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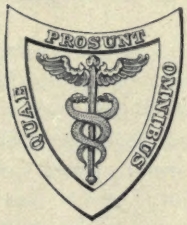

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SURGERY OF THE PROSTATE GLAND.[1]

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The subject of the surgery of the prostate gland is one that has vexed practitioners for generations, and is even now far from being in a satisfactory state. That advances have been made in treatment and many patients relieved of tortures worse than death itself; that operations once almost surely followed by death are now almost certain to succeed; that the profession is becoming more unanimous in regard to the indications for one operation rather than another in certain cases; and that an operation is no longer needlessly postponed until the patient has at least one foot in the grave—these are all signs of the ceaseless activity of the modern surgeon in searching unremittingly, conscientiously, and successfully for the greatest good obtainable for those unfortunates who come under his care suffering from the distressing effects of hypertrophy of the prostate gland.

That many patients will do well in a life of catheterism, while some will begin to fail immediately it is commenced, is a fact now well recognized, and it is the purpose of the present paper to urge an early resort to operative measures in those patients in the latter class, believing, as I do, that operation here, though necessarily an evil, is yet a less evil when undertaken early than when postponed until the last possible moment.

The rise of prostatic surgery has been well sketched by Gouley, and it is from his address that many of the following references have been obtained.

It appears that the ancients considered that patients with prostatic hypertrophy suffered from "excrescences" or "carnosities" at the

[1] Read before the College of Physicians of Philadelphia, April 6, 1904.

neck of the bladder, and that when these offered obstruction to the evacuation of the bladder, their destruction was attempted with metallic instruments, introduced, of course, through the penile urethra. The existence of the prostate gland was unknown until the middle of the sixteenth century, its discovery being attributed to Nicolaus Massa.

Riolanus was the first to suggest, in the early part of the sixteenth century, that the bladder could be obstructed by a swelling of the prostate. This surgeon in several cases of urinary retention successfully practised incision of the neck of the bladder through the perineum, but it is not recorded whether the cause was enlargement of the prostate gland.

John Hunter, Sir Everard Home, Brodie, and others, both recommended and practised tunnelling of the obstructing body by the catheter; but this remedy was finally abandoned as dangerous. Chopart records that when Astruc, ten years before his death, which occurred in 1766, was attacked by retention of urine, Lafaye attempted to introduce a catheter, but met with an obstruction from a tumor in the neck of the bladder. He therefore perforated this by a lance-shaped stylet introduced through the catheter, which was open at the end, and by this means succeeded in forcing the catheter into the bladder and drawing off the urine. The catheter was retained fifteen days. This false passage through the obstructing body persisted, and a catheter was introduced by it as occasion required through the remaining ten years of Astruc's life, and at the post-mortem examination the condition of the parts was found to be just as described. Chopart himself tried tunnelling of the prostate several times, but with fatal results.

Systematic compression, to maintain a patulous urethra, first proposed by Physick, of Philadelphia, was employed by Leroy d'Etiolles and Mercier; but probably its best known advocate was Mr. Reginald Harrison, of London, who employed olivary bougies, which were passed once in forty-eight hours or less often. The bougie was so shaped that the olivary swelling caused dilatation of the urethra and compression of the prostate as the instrument was passed into the bladder and again as it was withdrawn, it being allowed to remain in place for several minutes.

Perineal operations came into favor earlier than those by the suprapubic method, owing probably to the greater familiarity of surgeons with operations in the former region, due to the then widespread practice of perineal lithotomy. Covillard,[1] in 1639, successfully operated by perineal cystotomy and removed a hard mass, not a stone, crushing and destroying it during extraction with the forceps. Chopart describes how Desault, who died in 1795, after

[1] Sir Henry Thompson considered the "excrescence" a true tumor of the bladder, and not part of an hypertrophied prostate; but Gouley speaks as if it were prostatic.

removing a calculus by perineal lithotomy, found and twisted off a tumor in the bladder, and Sir William Blizzard several times before 1806 performed perineal prostatotomy for enlargement without any calculous formation. Such an operation, combined with lithotomy, was by no means infrequent in the early part of the nineteenth century, and was sanctioned by Sir William Ferguson, who employed this procedure even before 1848.

Amussat removed a calculous and a protruding mass of the prostate by suprapubic cystotomy before 1832.

But the first regular surgical procedure was established in 1834 by Guthrie, under the name of "division of the bar at the neck of the bladder," this bar being in some cases due to the enlargement of the two lateral lobes of the prostate drawing up a fold of mucous membrane across the vesical orifice of the urethra. He accomplished his purpose by a catheter carrying a concealed blade. Where marked prostatic enlargement coexisted he advised perineal prostatotomy, but it is not certain that he ever performed it. Mercier, whose name is pre-eminent in the early days of prostatic surgery, devised, in 1837, special instruments—called by Gouley prostatotome and prostatectome—and at later dates modified them in various ways. These instruments were used as the internal urethrotome is at the present time, through the penile urethra, without either a perineal or a suprapubic opening, and did not meet with very general favor. Leroy d'Etiolles, as well as Civiale, claimed priority over Mercier in the introduction of the operation since known by his name, but it appears that their claims are ill-founded.

A further improvement on Mercier's method was that introduced about 1873 by Bottini, who aimed to avoid the hemorrhage attendant upon Mercier's operation by the use of galvanocaustic apparatus. Gouley, however, states that the bleeding by Mercier's method was trifling, and that therefore Bottini's modification was unnecessary. Although there are occasional reports of cases treated by Bottini's method during the twenty years or more following his first description of it, yet they are by no means frequent until after the publication, in 1897, of the well-known paper by Freudenberg, in which he described many improvements in the requisite apparatus. This surgeon, four years later, recommended the addition of a centimetre scale to the shaft of the Bottini cautery, in order that the operator might have a more definite idea of the position of the beak of the instrument when in use. Further modifications of the galvanocaustic apparatus have been introduced by Dr. H. H. Young, of the Johns Hopkins University; he, with Willy Meyer, of New York, and Orville Horwitz, of Philadelphia, being among the most prominent advocates at the present time of this operation, to the practical exclusion of all others.

Meanwhile, various other methods of treatment had been introduced. Of these, the most important are those that arose from the

practice of tapping the bladder in cases of retention of urine where passage of the catheter proved impossible. Simple catheterization to relieve the bladder of its residual urine had long been employed; and it is interesting to note that the clever manœuvre of increasing the curve of the catheter by partially withdrawing the stylet as its beak approaches the obstruction was practised and taught by Physick, the Father of American Surgery, long before it was accidentally discovered by Mr. Hey. Where it was impossible to introduce the catheter the bladder was punctured, either suprapubically or through the rectum. It was feared that urinary extravasation in the former situation would be more dangerous, and hence the majority of surgeons preferred the rectal route, it being found in many instances that the channel thus formed served fairly well for voluntary micturition (even after the cannula was withdrawn) until the urethra again became patulous by the subsidence of inflammation. Perineal puncture, though practised during the seventeenth and eighteenth centuries, fell into disuse during the early part of the nineteenth, the rectal route being the favorite.

Thus arose the treatment by urinary fistula, and from the concomitant drainage of the bladder, it may be considered a distinct advance in therapeusis. Sir Henry Thompson narrates that he saw some patients of Mr. Thomas Paget, who had had their bladders punctured suprapubically, completely relieved of the tenesmus and other distressing features by wearing a cannula or a catheter in the suprapubic fistula, and that this sight gave him encouragement to try the effect of permanent suprapubic drainage, even in cases with no retention of urine. When a suitable case presented itself, he accordingly introduced a long curved sound through the urethra, and, making it impinge upon the wall of the bladder above the pubic symphysis, cut down upon it with a small incision, and introduced a tube. In many cases in which he employed this method the relief afforded was marked, but he later abandoned this plan of treatment for drainage through the perineum. Dittel, Keyes, and Swinford Edwards were among the other surgeons who recommended the suprapubic fistula.

An important improvement in the method of forming the suprapubic fistula was that introduced in 1888 by Hunter McGuire. This consists, in brief, in establishing a fistula through the abdominal walls obliquely upward from the bladder, so that the fistula "bears the same relation to the bladder that the spout of a coffeepot does to the bowl." By this procedure McGuire was able to completely relieve his patients of their cystitis and residual urine, no involuntary leakage occurring even in the supine position, and the patients, in some instances, being able to project the stream of urine in a parabolic curve to a distance of several feet by voluntary contraction of the bladder. The urine was retained for from two to six hours. Morris, of New York, in one instance clothed this fistulous

tract with skin by transferring narrow cutaneous flaps into the wound at the time of operation.

The treatment by perineal fistula developed as a natural consequence of perineal cystotomy, and was generally combined with an incision into the prostate gland. This was a method largely employed by Reginald Harrison, commencing in 1881, his first operation having been performed on November 4th of that year. He used a small perineal incision, opening the membranous urethra; then the prostate was incised, and a perineal tube was introduced and retained for from six to twelve weeks. If the natural channel was not restored the fistula persisted. Prof. Gouley, of New York, claimed priority over Harrison in the re-introduction of perineal prostatotomy, his first operation, in which, however, he left no instrument in the bladder, having been performed April 7, 1880, and his third operation, in which he left a large-sized rubber tube in the perineal wound, having been done in January, 1881. Whitehead was likewise among the earlier advocates of the treatment by a permanent perineal opening.

Excision of the obstructing parts of the enlarged prostate by suprapubic cystotomy was first widely advocated by McGill, of Leeds, in 1887, he having before this date practised permanent suprapubic drainage, which he preferred to that by the perineum. Belfield, in America, had done suprapubic prostatectomy before this time, his first operation being in October, 1886; Dittell had, in 1885, removed a portion of an obstructing prostate through a previously existing suprapubic fistula, which he enlarged for the purpose; Trendelenburg, in May, 1886, and Benno Schmidt, in August of the same year, had employed this route for removal of pieces of the prostate, but to McGill has always rightly been attributed the priority in bringing this procedure prominently before the profession. The most enthusiastic supporters of McGill's operation have been Buckstone Brown, Kümmel, Atkinson, Keyes, and Fuller. As originally practised, this operation consisted in cutting off, through the usual incision for suprapubic cystotomy, by means of scissors or rongeur forceps, twisting off with bladder forceps, strangulating with an écraseur, or crushing with a lithotrite, any projecting masses of prostate tissue. At times, also, portions of tissue, forming the so-called prostatic tumors, were enucleated with the finger, either alone or aided by the scissors or other instrument, from their position deep within the gland.

But to Freyer is undoubtedly due the credit of bringing before the medical world a plan of operation whereby an attempt is made to enucleate the whole of the enlarged prostate gland. Through a suprapubic incision he opens the bladder, and incises the mucous membrane overlying the affected gland by a cut parallel to the urethra, over each lateral lobe of the prostate. Then, by working merely with the finger, he states that he has been able to enucleate

the entire prostate, leaving the urethra intact. The technique of this operation will be discussed in greater detail on a subsequent page. Many other surgeons have assailed Mr. Freyer's claim to originality, and assert that he is laboring under a grave misapprehension if he thinks he is the first person to operate in this manner, insisting that his method is nothing more than the removal of very large prostatic tumors from the substance of the gland, leaving behind the outer margin of glandular substance which, by the growth of these tumors, has been compressed into a thin capsule-like layer. Thus, Wallace says: "The more rapidly growing areas (of the diseased prostate) increase at the expense of the more slowly growing ones, which are compressed and stretched over the surface of their quickly growing neighbors. By this process a capsule is formed, ill-defined at first, but later becoming very distinct. The elements forming this capsule show in process of time a lamellar disposition. The adenomatous mass can now be easily enucleated, and not only presents a smooth surface, but also leaves behind a smooth cavity." One prostate which he describes, removed post-mortem, showed within the layers of the "capsule" a small lenticular focus of glandular tissue. He concludes: "These facts seem to leave no reasonable doubt that the so-called total prostatectomy is nothing more than the removal of adenomatous masses."

It seems a pity that so many controversies in regard to surgical priority are so constantly arising, and it appears that prostatic surgery is particularly unfortunate in this respect. Riolanus bitterly denounced his contemporaries for claiming as their own operations which had been employed before their grandfathers were born and for a hundred years before that time. Mercier asserted that Leroy d'Etiolles has assumed not only the credit of operations which were not his own, but had also assumed a name not his own, since, in reality, Leroy came from Paris and not from Etiolles. Gouley spoke almost venomously against Mr. Harrison; and I think Mr. Freyer would be well able to reply to his critics as Mr. Harrison did to Prof. Gouley: "I see that Dr. Gouley claims priority for the proceeding just described; what is of more importance is that it has received his approval."

Prostatectomy by the perineal route, developing from perineal prostatotomy, has been supported by Dittell, Annandale, Harrison, Zückerkandl, Watson, Syms, Ferguson, Moore, Murphy, Bryson, and others.

The simplest perineal operation is done through a straight median incision. To gain more room, this has been supplemented by an oblique cut on each side, as advocated by Murphy, while Zückerkandl advises a transverse semicircular incision, with its concavity toward the rectum, which is separated from the anterior structures by blunt dissection, and Dittel aims to get still more room by an incision completely encircling the right side of the anus from the

coccyx and continued forward in the median line of the perineum; by this approach he is enabled to remove a wedge-shaped piece of each lateral lobe. The coccyx may be excised if necessary for completing the operation.[1]

Combined operations by the perineal and suprapubic routes have been advocated by Nicoll, who pushes the prostate into the perineum (whence it is removed) by the fingers of one hand introduced into the bladder through the suprapubic wound, and are employed by a number of operators at the present day, including Alexander and Guitéras, some of them removing the prostate through the perineum, and some through the suprapubic wound, using the counteropening to admit the fingers of the other hand to assist in the manipulations.

A mode of treatment by castration introduced in 1893 by J. William White, though widely employed by some surgeons for several years, is no longer in favor. Vasectomy, suggested as a less severe and mutilating operation by Mears, seems likely to continue in use for certain cases for a long time. The mortality from castration for enlarged prostate is at least 18 per cent., taking all cases together, and in selected cases has been reduced only to about 8 per cent. Castration for enlarged prostate was first performed by Ramm of Christiania, and has been advocated by Griffiths and Mansell Moullin.

Ligation of both internal iliac arteries, to induce ischæmic atrophy of the prostate, was proposed by Bier and employed by him in three cases, one of the patients, operated on intraperitoneally, dying from septic peritonitis. Willy Meyer employed this operation in two cases, the first patient recovering, after secondary hemorrhage and partial gangrene of the left foot, but the second died, apparently of renal disease. Those patients who survived (3 out of 5) are said to have had their bladder troubles more or less relieved.

Anatomy. In the human fœtus the prostate gland is a paired organ consisting of two lateral masses which coalesce around the first part of the urethra about the fourth or fifth month of intrauterine life. In some of the lower animals these lateral portions remain distinct and never unite in the median line. These facts have been known for centuries, and it was not until about one hundred years ago that Sir Everard Home took it upon himself to name as a "third lobe" that portion of the prostate lying above the ejaculatory ducts and behind the urethra. His experiences were apparently confined to an examination of four or five cases, the majority of which did not show any distinct third lobe. It is further worthy of observation that almost every author since his time has spoken of the "so-called third or median lobe" of the prostate as if there were reasonable doubt whether such a thing really existed.

[1] Perineal prostatectomy for malignant growths was employed in 1866 by Küchler, about 1870 by Billroth, in 1873 by Demarquay, in 1876 by Langenbeck, in 1882 by Spanton, and in 1883 by Leisrink. See Leisrink, Archiv f. klin. Chir., 1883, Bd. xxviii. s. 578.

Projecting into the prostate gland from the urethra is found the "uterus masculinus," which is the homologue of the female womb, being the persistent lower extremity of the Müllerian duct. This structure has a muscular and glandular wall of its own, and though in such close relation with the prostate, has no physiological connection with it; that is to say, the prostate gland, though composed largely of unstriped muscular tissue, can in no respect be considered homologous with the uterus.

Microscopically the prostate is found to be a compound tubular gland, its numerous acini being supported in a framework of connective tissue and involuntary muscle. The involuntary muscle is arranged in a rather compact layer around the periphery, and also at the site of coalescence of the two lateral lobes, above and below the urethra. The unstriped muscular fibres of the bladder wall are prolonged around the prostatic urethra as an inner longitudinal and an outer circular layer.

The whole gland is enveloped by a fibrous capsule distinct from the rectovesical layer of the pelvic fascia and formed by a condensation of the stroma of the gland. Outside of this fibrous capsule, and between it and the pelvic fascia, is found the prostatic plexus of veins, together with the arteries, lymphatics, and nerves distributed to the glandular structure. The venous plexus lies chiefly on the anterior and front lateral portion of the gland, receiving the dorsal vein of the penis.

Above, the prostate is in intimate relation with the urinary bladder, lying immediately beneath its neck, and being separated from its muscular walls only by a layer of fascia; below and posteriorly it impinges upon the rectum, connected rather firmly to this structure by a prolongation of the rectovesical fascia. In some instances the prostate gland has been found to envelope only about three-fourths of the calibre of the urethra, this canal merely grooving the gland upon its upper and anterior surface; but in the vast majority of cases the urethra appears to be channelled out of the substance of the gland, somewhat anterior to its mid-portion.

Besides the support it receives from the bladder and rectum the prostate is suspended in the anterior fibres of the levator ani muscle, called by Santorini the levator prostatæ, and anteriorly is supported by the puboprostatic ligaments, or true ligaments of the bladder (prolongations of the rectovesical fascia); while in the median line anteriorly, where the rectovesical fascia and the deep layer of the triangular ligament unite, the prostate is in relation with this latter structure, a levator prostatæ muscle being on each side.

Coursing through the posterior mid-septum, dividing the two lateral lobes, are found the ejaculatory ducts of the seminal vesicles and vasa deferentia. They empty into the floor of the prostatic urethra on each side of the caput gallinaginis, and posterior to the orifice of the uterus masculinus. The prostatic acini of each lobe

likewise empty into the prostatic urethra by eighteen or twenty ducts on their respective sides of the median line.

Where a projection into the bladder posterior to the vesical orifice of the urethra appears to arise from the prostate, it has been said (Griffiths) in some instances to spring from an accessory prostatic gland, which might then well be called a third lobe. But in the majority of cases such a growth may be and frequently has been traced to one or other of the two lateral lobes, being connected to them by a pedicle, much as a subperitoneal fibroid is attached to the uterus. It seems, indeed, not impossible that in those cases where it has been said that no such attachment could be found, the growth had finally torn its pedicle loose, and might in time even have migrated, as is not infrequently the case with analogous tumors of the uterus. Be these facts as they may, it is undoubtedly true that most surgeons at the present day are inclined to regard the third lobe as non-existent, that portion of the gland formerly called the third lobe, and lying between the two lateral lobes, above and posterior to the ejaculatory ducts, being recognized as merely the area of coalescence of these lateral lobes.

Etiology. The causes of enlargement of the prostate are still involved in much obscurity. Our ideas appear to have become less positive in this respect in proportion to the increase of our knowledge in other directions.

In the first place, nevertheless, practically everyone is agreed that there are two main pathological processes by which enlargement of the prostate gland is effected:[1] one by means of a tumor formation—a fibromyomatous, fibroadenomatous, or adenomyomatous change—and the second by a general increase in the size of the organ without distinct tumor formation. Both processes may coexist.

The tumors may be several in number, or there may be only one; they may arise in the substance of the gland or beneath its capsule. They may be composed largely of glandular structure, of muscular tissue, or of fibrous tissue; probably a combination of the first two is the most frequent, producing adenomyomata; the second in frequency of occurrence being the fibroadenomata, for in scarcely any instance is there any adenomatous tissue whatever.

Where general increase in size occurs, approaching more nearly a true hypertrophy, the fibrous is usually the predominant tissue, and it is this type of enlargement which is, as a rule, the cause of the stony hardness observed in some prostates.

To ascertain the underlying causes of the enlargement, whether neoplastic or hypertrophic, affecting the prostate, a number of theories have been proposed. These may all be reduced to two classes, in one of which the enlargement is held to be primary—to

[1] Griffiths thought that the adenomatous change was merely the first stage, of which fibrous overgrowth formed the final change, Journal of Anatomy and Physiology, 1889, vol. xxiv. p. 236.

be itself a cause—to arise *de novo;* and in the other of which it is considered a secondary change—as the result of some other process—as, perhaps, a misdirected compensatory hypertrophy.

To be strictly sincere, it does not appear to me that it is a matter of very great importance under which of these two theories we enlist our intellect; for it is, after all, a matter of purely academic interest, and for practical surgeons will remain such until some happy discovery will reveal the true cause of tumor formation in general, or the reason why at a certain age the bodily powers begin to fail and the tissues to become sclerotic.

To my mind those prostates which show tumor formation are to be classed with other tumors, which were formerly defined as discontinuous, purposeless hypertrophies of no known cause; while those glands which show only general hypertrophy are classed with other changes incident to age. The discussion of the causes has, I think, been much confused by the neglect of writers to keep these two classes distinct. Guyon and his school, who held that such enlargement was merely a part of a general senile change, appear to me to confine their considerations to the latter class; and here, too, may be placed the theory of Harrison, that the hypertrophy results from a vain effort to empty a bladder whose base has previously descended into the pelvis below the level of the urethra.[1] While, on the other hand, Velpeau, Paget, and Billroth, with their followers, who maintained that these phenomena were due to a myomatous change strictly analogous to that found in the uterus, evidently fixed their attention exclusively on cases of what I have called the first class, which is, in fact the larger.

In discussing the clinical causes, also, it is well-nigh impossible to avoid theorizing, since, as I have said above, so little is accurately known of the causes of this affection.

Race does not exert a very marked influence; the negro race is probably slightly less predisposed than is the white (Conner), and among the natives of China and Japan prostatic troubles are considered to be extremely rare. In India and Turkey, however, they are comparatively frequent (Wishard).

Age appears to exert a very marked influence. It is rare for any symptoms to be produced by an enlarged prostate before a patient has reached the age of fifty years; but Dr. Mudd has seen cases in a young negro, aged twenty-seven years, in a child, aged five years, and in an infant, aged thirteen months. The researches of Thompson and others have shown that appreciable enlargement exists in about one-third of persons over sixty years of age, but that it produces manifest symptoms in only about one in every twenty. For prostatic enlargement to appear first after the seventieth year is very

[1] Were this theory correct, a cure might be hoped for, in cases not too far advanced by a ventrosuspension of the bladder.

unusual. In natives of India and other tropical climates it appears much earlier, as a rule, the span of life being about fifteen or twenty years shorter than ours.

Social habits exert some influence. The gouty, those who have been addicted to the excessive use of alcoholic beverages, or who have been high livers in other respects are believed to form a large proportion of these patients. Why this should be so; why such a life should produce enlargement of the prostate gland, has not been determined. Excessive sexual indulgence has been held responsible in some instances, the overexercise of the gland being thought to lead to hypertrophy, just as Harrison thought hypertrophy ensued from constantly recurring efforts to empty an atonic bladder. This "prostatic overstrain," so named by Lydston, has been explained in the following way by Harrison: "That the withdrawal of a portion of that function of the prostate in which it has been the most vigorously engaged, should be followed by a continued activity in which growth is substituted for secretion, is not, I consider, pathologically illogical." McGuire held that, although prostatic overstrain might be the true cause of the enlargement, yet it was the senile sclerotic changes in the bladder which first caused the enlarged prostate to give symptoms.

Preceding inflammations, such as gonorrhœa, acute or chronic prostatitis, or prostatic abscess, may also be the starting-point of chronic enlargement of this organ.

Chronic passive congestions, finally, as in other organs, may lead to prostatic enlargement as well. Old men with cirrhotic kidneys and liver, with hemorrhoids or with varicose veins in the legs, are very apt to be sufferers from this malady.

Clinical Pathology. As the prostate gland enlarges, whether from tumor formation or as the result of a general hyperplastic process, various changes are produced in the bladder, the urethra, and the rectum. The usual direction of greatest enlargement is parallel to the urethra and posteriorly; that is, in the direction of least resistance, toward the base of the prostate, and away from the triangular ligament, this latter attachment of the prostate being practically a fixed point. The bladder cavity is likewise usually encroached upon, the vesical mucous membrane being raised posterior to the orifice of the urethra, and a pouch forming behind this projection. If the two lateral lobes enlarge in nearly equal degree, a mere fold of mucous membrane may be raised across the neck of the bladder just behind the vesical opening of the urethra, but some little distance in front of the ureteral openings. This fold constitutes the most usual variety of "bar at the neck of the bladder."

As the lateral lobes enlarge the prostatic urethra becomes lengthened, sometimes measuring as much as four inches, instead of barely an inch, which is the normal; and the curve is also much increased from the height to which the inner opening of the urethra is raised.

If one lobe enlarges more than the other the urethra is correspondingly deflected toward the less enlarged side. Where a submucous tumor projects into the floor of the bladder, at or near the median line, the urethral channel may become Y-shaped, and the catheter will pass now to the right, now to the left of the projecting mass. Finally, where the anterior commissure, or isthmus of the gland, enlarges as well,[1] there may be a collar formed around the vesical orifice of the urethra, which may then appear as a dimple, deeply seated near the centre of the prostatic mass.

At times where no intravesical growth at all is found, or after any such has been removed, it has been found still impossible to introduce a catheter through the urethra, the obstruction then being due to irregular projections into the floor of the prostatic urethra. This circumstance has probably been the cause of many failures to restore voluntary micturition after the old operation of McGill.

The calibre of the prostatic urethra sometimes becomes so much increased from the irregular enlargement of the prostate that it may contain an ounce or two of urine, and the unwary may be deceived into thinking the bladder has been reached by a catheter, which merely empties this little collection of urine in front of the real obstruction. On the other hand, the whole prostatic urethra may be compressed into a slit-like channel, impervious to fluid except when distended by an instrument. The vesical orifice may assume a crescentic shape, the concavity of the crescent being directed toward the area of greatest enlargement.

If the enlargement proceed chiefly toward the rectum that channel may be obstructed, and much difficulty in defecation ensue; while hemorrhoids may arise either consecutively or from a common cause.

Ordinarily, the first consequence of the almost invariable post-prostatic pouch formation is the presence of residual urine—or that urine which the patient is unable to expel by his voluntary efforts. Unless the prostatic enlargement is arrested, the amount of residual urine gradually increases, owing both to the increasing obstruction and to the decreasing muscular tone of the bladder, which becomes weakened by straining and overdistention. Ammoniacal decomposition of the urine, with consequent cystitis, quickly supervenes and gives rise to what is commonly the first symptom, namely, increased frequency of micturition.

As the residual urine accumulates the vesical orifice of the ureters may first become compressed, preventing the periodical discharge of their contents into the bladder and causing circulatory disturbances in the kidneys; while at a later period they may become dilated, along with the stretching of the rest of the bladder wall, so

[1] Dr. Murphy denies that this portion of the gland is subject to enlargement. Journal of the American Medical Association, March 29, 1902.

that they are no longer protected by a valve, but are in direct communication with the bladder, the backward fluid pressure reaching even the renal tubules. Finally, when the bladder becomes overdistended, a condition of urinary overflow may occur, and the patient will be forced to pass a drachm or less of urine every ten or fifteen minutes, or will suffer from a constant dribbling throughout the twenty-four hours. The combined backward pressure and septic changes in the urine produce renal disease, and this, in turn, reacts on the composition and quantity of urine.

The bladder may not, however, dilate; its walls may become much thickened, corrugated, and pouched; its cavity may even contract, or may be nearly completely filled by an adenomatous prostate. But, as a rule, where an adenomatous change occurs in the prostate the bladder dilates; whereas, if the prostate be a hard fibrous mass, and comparatively small, the vesical walls are contracted and thickened.

The weight of the diseased prostate varies from one to twelve ounces; yet the largest in bulk may not weigh as much as one smaller but more compact.

Uric acid, or phosphatic calculi, frequently form in the puddle of residual urine, and much increase the suffering of the patient. Hemorrhage may thus be accounted for.

Symptoms. The symptoms of prostatic enlargement may be conveniently considered under the heads of those of which the patient complains and those which the surgeon discovers on examination.

The patient will probably for a rather indefinite time have been affected, perhaps without paying much attention to it, with difficulty in starting his stream of urine; the urine when started will have been expelled with little or no force, tending to drop vertically from the meatus, not spurting forth in the normal parabolic curve; a longer time than usual will have been occupied in emptying the bladder, and at the conclusion of the act of micturition there will have been considerable dribbling of urine, no power existing to void the last drops in spurts. The stream will probably not be smaller than in health unless stricture exists as well.

But probably the first deviation from normal which will have forcibly arrested the attention of the patient will have been the necessity of arising once or oftener during the night to evacuate his bladder. This increased frequency of micturition may also have annoyed him during the day, but is less noticeable then that at night. The bladder may become so extremely irritable that no sooner will any urine have been discharged into it from the kidneys than an uncontrollable desire to empty the bladder will arise, and thus the patient will be reduced to a most miserable state, being impelled to urinate every ten or fifteen minutes, and his general health in a very short time showing the effects of this constant unrest. On the other hand, the residual urine may gradually accumulate without causing such

severe distress, and a state of retention with overflow finally develop. Besides the cystitis thus manifested by crebruria, a feeling of weight and distention in the perineum may exist, and piles, with prolapsus ani, from the consequent tenesmus, may ensue.

The patient may consult a physician before this stage is reached, or he may not be disturbed sufficiently to think this necessary until some exposure to cold, some indiscretion in diet, or some other irregularity in his life has brought on an attack of acute retention of urine. Thus, when first seen by the physician he may present a bladder distended nearly to the umbilicus, he himself not being aware that residual urine had been accumulating for perhaps months past. Hence, the first physical sign to be looked for in patients suspected of prostatic troubles is a hypogastric tumor, with the characteristics of a distended bladder. It is especially important to detect this before introducing a catheter in cases where chronic retention has probably existed for a long time; for, as is well known, the complete sudden evacuation of such a bladder is, as a rule, speedily followed by the patient's death.

The patient should next be requested to urinate, when much information may be derived from the character of the stream, in accordance with the changes noted above. If it is apparent that no excessive amount of residual urine exists, it will now be advisable to introduce a catheter, noting the presence of strictures, the distance of the vesical orifice of the urethra from the meatus, and any changes in the curve or deviations from the right line of the subpubic urethra. Then the amount of residual urine is determined, not being deceived by the ounce or more which may, in rare instances, flow from the dilated prostatic urethra. While the catheter or a sound is still in the bladder a finger should be introduced into the rectum, when, by careful manipulation of the one and palpation with the other, a fairly accurate idea can be obtained as to the size, form, and density of the prostate. The condition of the bladder walls, whether rugous and contracted, coated with phosphates, thickened, or dilated and overstretched, can also be ascertained, as well as the existence of a calculus.

If an obstruction to the catheter be encountered within less than seven inches from the meatus, it is in all probability due to a stricture and not to the prostate; but if the obstruction be easily overcome by sharply depressing the handle of the instrument, if of metal, or by slightly withdrawing the stylet, if of webbing, the obstacle is almost certainly an enlarged prostate.

Diagnosis. The symptoms and physical signs being well known, a diagnosis is not, as a rule, difficult. The most important affections with which enlargement of the prostate may be confounded are: atony of the bladder; cystitis, especially chronic; stricture of the urethra; vesical calculus; tumor or tuberculosis of the bladder, and malignant disease of the prostate or some neighboring structure in

the pelvis. By symptoms alone no one of these can be definitely excluded, but by careful attention to the clinical history, combined with painstaking physical examination, I believe that in almost every case a correct diagnosis can be reached.

In atony of the bladder arising from other causes the existence of an enlarged prostate may be readily excluded by combined exploration with an intravesical sound and a finger in the rectum, while in uncomplicated cystitis these same marks of difference hold good, and there is, moreover, no residual urine.

In stricture of the urethra the obstruction, as stated above, is almost invariably within seven inches of the urinary meatus, and an enlarged prostate may be excluded by the means of examination already indicated. In case, however, of an impermeable stricture with chronic retention it will not be possible to satisfactorily examine the prostate until these conditions are relieved.

Where a vesical calculus exists it is not liable to be mistaken for an enlarged prostate unless it is both encysted, and so thickly coated with mucus that no grating sensation is imparted to the sound. But even under such circumstances there may be no residual urine, which is, as already insisted upon, a nearly invariable accompaniment of every enlarged prostate producing symptoms, and there will probably not be the characteristic change in curve of the subpubic urethra. If the calculus be prostatic, or even if it merely coexist with an enlarged prostate, a positive diagnosis is more difficult. Bleeding is more common in cases of calculus than in those of enlarged prostate alone, and the pain is less constant and more confined to times when the bladder contracts upon the concretion or when the patient is actively moving about. The greatest frequency of urination, also, is during the day, and the patients with stone are not, as a rule, disturbed much at night.

Probably the most difficult diagnosis of all is that from polypoid growths in the bladder, which, when springing from the region of the prostate, may very closely simulate a pedunculated tumor of this organ. But in nearly all other forms of vesical tumor other than prostatic, hemorrhage is an early and conspicuous symptom, and is usually not attended by much pain.

Tubercle of the bladder is probably always secondary to similar disease elsewhere in the body, most often in the epididymis. While the vesical tenesmus may simulate that present in cases of enlarged prostate, physical examination with sound, finger, and cystoscope, and careful examination for tubercle bacilli and the application of the tuberculin test will usually reveal the true state of affairs.

Malignant growths of the prostate itself can be distinguished from benign enlargement of this organ only by the tendency they exhibit to infiltration if of carcinomatous origin, or to rapid growth and the production of cachexia if of a sarcomatous nature. Compared to the benign overgrowths they are distinctly rare.

PROGNOSIS. A question of considerable importance and much interest in connection with enlargement of the prostate is that of prognosis. In few other diseases is it so necessary for the surgeon to know what may be accomplished by the various methods of treatment possible, and in probably no other class of cases is the surgeon blamed more severely for errors in judgment. It is not sufficient, indeed it is neither ethical nor humane, to hope that the patient will die of some intercurrent affection before any necessity arises for instituting active treatment on behalf of his enlarged prostate; and hence every physician or surgeon who has such cases under his care must give careful thought and attention to each individual patient, and must know whether the expectation of life will be lengthened or decreased by the treatment he purposes undertaking, or whether the certainty of a life of considerable discomfort for a longer time is not less to the patient's ultimate advantage than the risk to life incurred by a rather severe and shocking operation, which, if successful, will enable the patient to live out his natural term of life in ease and comfort.

There are, then, two main questions to be solved in this connection; first, whether the patient's life can be saved, prolonged, or, at least, not sacrificed, by the treatment to be pursued; and second, whether his sufferings will be relieved wholly or in part, or whether no change at all can be obtained.

Under medical treatment and catheterism there is practically no possibility of directly terminating the patient's life; with the understanding that every antiseptic precaution be taken in catheterization, his life may be prolonged, and, in certain cases, made very comfortable.

Many a patient who has to pass a catheter only once or twice in the twenty-four hours will live a life of perfect ease, and will round out his days without interruption. But, where the catheter has to be passed frequently, that is to say, as often as four to six times in the twenty-four hours, or where its passage at even longer intervals is attended with pain or difficulty, catheterism must be considered at the present day an insufficient remedy, except in those who are already on the threshold of the grave. The expectation of life, moreover, in patients treated by catheterization has been shown by Harrison and Lydston to be, in the average, not more than four or five years.

The next mildest form of treatment is drainage of the bladder. By this means may be obtained relief of the cystitis, and, consequently, of the tenesmus, pain, and general unrest, in a certain number of cases. In my opinion, it is applicable chiefly to those in a very debilitated condition or to the very old. Drainage by a permanent catheter introduced through the urethra can rarely long be endured, and is usually only to be employed in preparing the bladder for radical operation.

Cabot,[1] in an article on the effect of drainage on the kidneys in nephritis, makes some observations of very great interest in connection with the treatment of prostatics. Starting with the proposition that urinary obstruction from enlarged prostate or other cause produces increased renal pressure, which may even reach to the Malpighian glomerules, and that this pressure alone, even without infection, will result in fibrous changes (interstitial) in the kidneys, as well as in an increase in quantity and a decrease in specific gravity of the urine excreted, he goes on to show by the report of six cases that the invariable result of relief of the obstruction was to bring the urine back to a more nearly normal state. Especially noticeable was this result in cases where even the greatly increased secretion of urine had been ineffectual in "carrying off the waste products in sufficient amount" and where uræmic symptoms had appeared.

He is well aware, he states, that this procedure is no new therapeutic measure, but he thinks its applicability to renal disease has not hitherto been sufficiently appreciated, although the good effects of Edebohls' operation in relieving renal tension are well known to the profession. Those authors as Langlois, he adds, who have noted the decrease in size of enlarged kidneys succeeding upon bladder drainage, have thought it was due to either relief of congestion or to the emptying of hydronephritic pouches.

Dr. Cabot says that for the purpose of the present investigation he has "taken it for granted that a patient with obstructive disease of the prostate and dilated bladder may be regarded as having some degree of interstitial nephritis if the urine is abundant and of very low specific gravity. If such a patient is suffering from anorexia, nausea, and dry mouth, either with or without psychical disturbances, these are to be looked upon as symptoms of uræmia due to this interstitial nephritis. If, in addition to these symptoms, he has a high fever and the urine contains pus, it is to be regarded as probable that he has pyelonephritis." By instituting continuous drainage and by flushing out the urinary tract with large draughts of water, he has succeeded in promptly relieving such symptoms.

The time during which this constant drainage must be continued varies with the individual patient; by discontinuing it soo soon, the renal and uræmic symptoms were found to promptly recur, but by persisting in this treatment until the urine was nearly normal in both quantity and quality, his patients returned to a life of intermittent catheterization (when they declined operative interference) in the enjoyment of excellent health.

Dr. Cabot further insists that the dangers of sudden emptying of a chronically distended bladder are much mitigated by the constant drainage instituted; for he has found that although considerable hæmaturia might ensue for a few days, yet that this neither in any

[1] Boston Medical and Surgical Journal, 1903, ii., p. 559.

way interfered with the perfect drainage, nor was it followed by increasing uræmic symptoms, as is usually the case when such a bladder is emptied and no constant drainage established.

The first case reported is that of a man, aged sixty-seven years, who, after using the catheter for some months, there being over twelve ounces of residual urine, was taken severely ill, with a temperature of 103° F.—apparently commencing pyelonephritis. By constant drainage the amount of urine was, in the course of some weeks, reduced from 60 or 70 ounces to less than 50 ounces daily, while its specific gravity increased from 1007 to 1023. Intermittent catheterization was then instituted.

In the second patient there was anorexia, dry mouth, much nausea, and marked somnolence. By constant drainage the return to normal was remarkably rapid.

The third patient, in much the same general state, had fever as well; his bladder also was distended nearly to the umbilicus. Thirty-seven ounces of urine of very low specific gravity were withdrawn, and by continuous drainage, in a period of two months, the patient's health was practically restored, the quantity of urine, however, remaining at 70 to 90 ounces daily, and its specific gravity being about 1008.

The fourth patient, aged seventy-two years, had suffered for several years with crebruria, there being about 12 ounces of residual urine. A resort to catheterization once or twice daily produced, in about two weeks' time, symptoms of commencing pyelonephritis. Constant drainage was then begun. Hæmaturia occurred, and the next day the patient became uræmic. Under proper constitutional treatment all unfavorable symptoms disappeared, but it was not until the seventy-ninth day that intermittent catheterization could be substituted for continuous drainage. His daily urine remained at about 100 ounces, of specific gravity 1012 to 1015.

In the fifth patient the chronically obstructed bladder contained 40 ounces of urine. Constant drainage, while it produced transient hæmaturia, relieved the delirium, fever, and thirst. Three weeks later intermittent catheterization was begun. The urine at last report, over a year after the acute attack noted above, was 40 to 60 ounces daily in quantity, of specific gravity 1017.

The last patient reported was in the early stages of chronic nephritis, with polyuria amounting to 8 pints in the twenty-four hours. When chronic retention set in this amount was reduced to 6 pints, of specific gravity 1005. Constant drainage was instituted, and in one day the amount of urine drained off reached 16 pints. This was gradually reduced to 6 pints, and, finally, to 4 pints daily, while the specific gravity rose to 1012 and 1015.

The success of Thompson, McGuire, and others in treating these patients years ago by means of suprapubic permanent drainage, and of Harrison by means of a perineal tube, should not be forgotten

at the present day; and, while we recognize the inadequacy of such methods to restore the patient to his normal condition, yet, in a limited number of cases, they are still useful. Especially is this so in patients with very bad cystitis and where some immediate relief is imperative. In such cases so radical an operation as prostatectomy will almost surely kill, unless time can be obtained to relieve the cystitis, to get the kidneys into fair condition and to improve the general health of the patient. In patients such as these the formation of a permanent suprapubic fistula by McGuire's method, or, if the prostate be not too large, simple perineal prostatotomy with the introduction of a tube will afford almost certain relief to the urgent symptoms, and in many instances will enable the constitution to withstand prostatectomy at a later date. Neither castration, vasectomy, nor ligation of the internal iliacs will act sufficiently quickly in such cases; indeed, in my opinion, these operations are no longer to be considered desirable under any circumstances.

References which I have to 107 cases treated by McGuire's method show only 2 deaths; so that even in the most serious cases it will be exceedingly unlikely to precipitate a fatal termination.

The Bottini operation is not one for the general surgeon, nor, to my mind, for the average patient. On the surgeon's part it requires a technical knowledge, which, even in the hands of those known to be the most skilful in its employment, has not sufficed to prevent fatal complications. The greatest points in favor of galvanocaustic prostatotomy are its low mortality (4 to 6 per cent.), and the fact that if it fails to relieve after the first application it may be repeated once or several times with little more risk than attended its first employment. Moreover, the patient has still a prostate left whose removal by excision may effectually cure him, even when several applications of the Bottini cautery have proved ineffectual. On the patient's part, this operation is often welcomed for these very reasons: that its danger is comparatively slight, that general anæsthesia is not required, that no "cutting" is to be done, that no external wound is left for healing, and that it does not interfere with subsequent operative treatment by other methods.

But with all the advantages claimed for it, Bottini's operation is first and foremost a makeshift, quite as much as castration or McGuire's suprapubic fistula. It does not remove the offending organ. It burns grooves in it, and the surgeon leaves sloughs to be cast off into the bladder, and then waits, hoping that the cicatrization of his sloughing sores will diminish rather than increase the deformity. It is an operation done practically without the aid of either sight or touch; it is nearly impossible to know how long, how wide, or how deep are the grooves burned, or whether they are being burned in the prostate or in the bladder wall; and it is absolutely impossible to know what has been accomplished in the destruction of prostatic tissue or that the prostate will not again grow into an

obstructing position. Moreover, it is an operation wholly inapplicable to emergency cases and to patients with urethras impassable from either strictures or prostatic obstruction. It is, therefore, in my opinion, an operation only to be employed when (1) prostatectomy is inadvisable or is refused, or when (2) the urethra is freely open to instrumentation, there is no cystitis, and little residual urine.

We are reduced, then, to prostatectomy as the operation of first choice in all cases in which it is not contraindicated. When done by the method of Freyer, that is, by suprapubic enucleation with the finger, passing between the capsule and the sheath, the mortality is decidedly lower than by the method of McGill. In 12 cases of the former operation, Mr. Moynihan had only 1 death, and in 51 cases Mr. Freyer had 5; Barling, however reports 10 cases so treated, with 3 deaths, making, with 6 successful operations recorded by McRae and by Stoker, a combined mortality rate of less than 12 per cent. for the 79 patients; while the statistics of Belfield and of Mansell Moullin show, respectively, nearly 14 per cent., and over 20 per cent. for McGill's operation. Recent cases of McGill's operation, reported by Armstrong, Horwitz, Fuller, and Thorndike, show a death rate of over 21 per cent. among 28 cases. The mortality in 73 recent cases (Albarran, Deaver, Ferguson, Horwitz, Murphy, Syms, Verhoogen) of perineal prostatectomy is only a little over 8 per cent., but the results have not, as a rule, been nearly so good as those achieved by Mr. Freyer's method. Forty-six out of fifty-one patients treated by this latter operation are reported by him as having their urinary function restored to its natural condition.

Mere figures, therefore, are decidedly in favor of Freyer's operation; but both from what I have read in the reported cases of others and from my own experience, I am convinced that it is not the best operation in every case, even if it be possible. Mr. Freyer reports a case in which he attempted his own method, but owing to the density of the gland and its firm adhesions to the rectovesical fascia, he was able to remove only pieces of it. This patient died on the second day after operation of heart failure, and the bladder was found full of clots, the hemorrhage during the operation having been free. Now, it does not appear to me to be strictly sincere to argue that Freyer's operation gives a mortality of less than 10 per cent. when we exclude cases in which it was attempted but found impossible of performance. As well might we give a certain mortality for the operation of ovariotomy, considering only those cases where the adhesions to the intestines were few and light, and where the cyst shelled out easily, yet exclude those cases where a prolonged and delicate dissection was necessary to deliver the cyst, claiming that such cases form a class of themselves. Such a method of calculation would only lead others astray and encourage us in self-deception, a thing Mr. Freyer himself would be very far from countenancing.

Certainly, everything within my own experience convinces me

that while Freyer's method of prostatectomy is by far the best operation for all cases to which it is applicable, yet that there is a small and limited number of cases in which it is neither advisable, nor, as Mr. Freyer's own patient above referred to, plainly shows, at all possible.

The perineal operation I have employed a number of times, and have found it quite satisfactory in certain cases, but for some years have largely abandoned it for the operation of complete suprapubic extirpation, which I find in my own hands gives better functional results, is attended by a less mortality, and is certainly easier of performance. Of course, we know that mere facility of execution for the surgeon is no argument in favor of one operation, if another, even if much more tedious and intricate, would assure a better result to the patient; but the greater ease in the suprapubic operation consists, not alone in mechanical execution, but in economy of time and less distortion of the neighboring parts, both of which are considerations of importance in the class of patients under discussion.

TREATMENT. The treatment, therefore, of prostatics—a convenient term adapted by Belfield from the German *Prostatiker* and the French *prostatique*—resolves itself into a choice of remedies, not into any hard-and-fast rules which may not be transgressed. It has well been said that he is either a fool or at best a surgeon of very limited experience who knows of only one method of treatment for a certain class of cases; and while I myself maintain that prostatectomy by the suprapubic method of Freyer is the best treatment, I do so with the distinct reservation that it is not immediately applicable to every case.

Having seen, then, in the preceding pages the relative dangers and probabilities of ultimate success from the various methods of treatment applicable, it is next requisite to attempt an expression of some general rules which may guide the surgeon in selecting his course of treatment.

A healthy man somewhat under sixty years comes to you with the simple complaint that he finds it necessary to rise once almost every night to pass his water; that this is becoming, he thinks, a more invariable habit; that he has waited, thinking matters might return to their former state without treatment, but that he fears they are growing worse. In such a case as this, after finding the cause of his trouble to be a moderately enlarged prostate, and determining the amount of residual urine to be trifling—one or two ounces—I would recommend the passage of a soft rubber catheter, with strict asepsis, every night at bedtime. It is probable that the bladder being thus emptied, no call during the night would arouse him, and it is barely possible, though I admit very improbable, that with good hygienic surroundings and a regular life, the bladder might acquire sufficient tone to expel the residual urine, and that no further trouble would ensue. More likely is it that catheterization, at first employed only

once in the twenty-four hours, would soon, say in the course of six months to a year, be resorted to twice or even three times in a similar period, to obtain relief from the vesical tenesmus, and that from this constant use, cystitis, if only of a mild degree, would have developed. At this period of the disease it is important to undertake more active measures before the general health is impaired. In cases such as this very many surgeons would be disposed to recommend the Bottini operation—a trifling risk; no cutting, no external wounds to heal; a prostate not very large, nor causing much obstruction; possibly no impairment of the generative function as a result of the operation. The patient would be more inclined to accept such a proposition than one of radical extirpation of the gland, even though he were told that one operation by Bottini's method was not a sure cure, and that even after two such operations the prostate might still continue to enlarge. In my opinion, if the prostate gave evidence of rather rapid increase in size, showing it to be probably an adenomatous gland, a Bottini operation would not be for the best ultimate good of the patient; I would advise him to have a suprapubic prostatectomy done by Mr. Freyer's method. The prostate would probably continue to enlarge, even if temporary relief from the residual urine had been obtained by the galvanocaustic operation; and the patient would in time be forced to submit to a radical operation when periprostatitis had rendered complete extirpation impossible, when his bladder had become weakened, his kidneys diseased, and his general constitution impaired. If, on the other hand, the prostate in such a case appeared to be a small fibrous mass, not increasing in size, but obstructing the urine by pressure on the prostatic urethra, I should feel less disinclined to try the effects of a Bottini operation. This latter class of patients is distinctly rarer than the former. In the former case the prostate could almost certainly be removed in its capsule from within the sheath of the gland, with comparatively little hemorrhage and with practical certainty of no recurrence. In the latter case, however, the prostate would probably be densely adherent to its sheath; an attempt at extirpation by the suprapubic route would probably be difficult, bloody, and prolonged; the gland would have to be removed in pieces, not insuring its total ablation. but perhaps producing serious and lasting injury to the vesical sphincter. A perineal operation, removing the floor of the prostatic urethra and allowing the isthmus of the gland above the urethra to remain, would here, I think, be attended by better results than a suprapubic operation.

Suppose, now, a second case, similar to that just discussed, but in an older man, from sixty-five to seventy years of age. What treatment is to be pursued here? If his constitutional condition be as good as was that of the patient just mentioned, I would employ a similar treatment, and advise suprapubic prostatectomy under the same conditions, but at an earlier date. If postponed too long the

health of a patient at such an age may rapidly fail, and any operation prove too late or too great a risk to save his life.

In a third case the patient may first come to us after he has been using the catheter for months or years. He may apply because of the greater frequency with which the catheter must be used, because of the greater pain and difficulty attending its introduction, or for both reasons. In any circumstance, he probably has severe cystitis and impaired kidneys. If drainage by a permanent catheter through the urethra, combined with the internal administration of urinary antiseptics, washing out the bladder, and careful diet, effects an improvement in these particulars, I would not hesitate to resort to Freyer's operation as the surest method of saving his life and restoring his urinary function, providing the prostate were adenomatous. If no improvement in the cystitis was apparent, I would at any rate open the bladder either suprapubically or through the perineum, and direct my further treatment in accordance with what I then discovered by sight and touch. If the bladder before operation appeared to be small and contracted and the prostate hard and not very large, I should open the perineum, and at least drain the bladder, and at the same time remove so much of the offending organ as the condition of the patient and the state of the parts appeared to countenance. If the bladder appeared to be dilated and the gland adenomatous, I should prefer the suprapubic route, completing the operation by Mr. Freyer's method, if possible, but at least draining.

If drainage only had been instituted, three terminations to the case present themselves: (1) The patient dies from the progressive asthenia and nephritis, in spite of the drainage, or he recovers (2) sufficiently satisfied with a permanent urinary fistula to seek no further treatment, or, finally, (3) he still requires a prostatectomy, which now, in the absence of cystitis, can be performed with little danger.

Still another case may occur: A patient, old, feeble, perhaps delirious, has chronic retention of urine, the urethra not being permeable to instruments. Hemorrhage from the urethra, and perhaps into the bladder, complicates the case. Evidently the patient is in a critical condition. Strictures may make matters worse. At all events, the existence of an enlarged prostate is definitely determined; but the history throws little light on the primary cause of the urinary retention. What is to be done? Castration, ligation of the internal iliacs, the Bottini operation, suprapubic or perineal prostatectomy are all discarded, some as futile, some as preposterous, others again, as entailing far too great shock. The only thing left to do is to drain the bladder. I do not think simple aspiration in such a case as this will be of any lasting benefit, but rather that it will do harm by relieving the tension and encouraging vesical hemorrhage, which, in turn, only makes matters worse. To relieve the

immediate distress of the patient it may be advisable to thus draw off his urine, but it is idle to hope that the obstructions in the urethra will subside soon enough for permanent drainage to be available by that channel, and, in my opinion, the surgeon had best proceed at once to a suprapubic cystotomy. Such an operation can, if necessary, be done under local anæsthesia from cocaine, and does not involve an incision into the prostate, which would be necessary in a perineal cystotomy, and which would much increase the risk of hemorrhage. The bladder being opened, any vesical oozing could be controlled with hot solution. If the patient did not react from the serious condition in which he was at entrance, his death would at any rate have been rendered easier, and he would have been afforded the only chance to recuperate which surgery has to offer. As in the former case considered, a recovery from the cystitis, with persisting debility from the enlarged prostate, would be an indication for prostatectomy; or if such an operation appeared to be too severe, a Bottini operation, which could be done through the urinary fistula if preferred, might be undertaken, with a fair probability of relief for the few remaining years of life.

Technique of Special Operations. *Perineal Prostatectomy.* The patient being placed in the lithotomy position, a medium-sized steel sound—one that will pass readily through the urethra—or a Ferguson's prostatic depressor, is introduced into the bladder, and a straight median incision is made in the perineum from the base of the scrotum to a point near the margin of the anus, of course not dividing the sphincter. The membranous urethra is then exposed in the usual way, and, if preferred, may be opened. The dissection is then continued, dividing the anterior fibres of the levator ani, which are drawn to each side with hooked retractors, and the sheath of the prostate thus exposed. The rectum and its overlying tissues should be pressed backward with a blunt retractor, opening up a fairly large space in the recto-urethral triangle. By the sound or Ferguson's depressor, inverted, or with a finger passed into the bladder through an opening in the membranous urethra, the prostate can now be pressed downward and outward, stretching the process of rectovesical fascia composing its sheath. When this is incised the separation of the prostate from the surrounding structures should be begun at its posterior part, and the operator should work forward. In this dissection, which is by no means as easy as the shelling out of the gland in the suprapubic operation, I have been greatly aided by the use of Murphy's hooks, a full set of which I now regard as indispensable to the proper performance of this operation. By them each lobe of the gland is in turn drawn toward the operator and separated from the bladder. The floor of the prostatic urethra may always be removed, but the upper or anterior commissure of the gland may well be left behind, since in the class of cases in which I recommend this operation there is little likelihood of its

causing any subsequent trouble. Nor will there usually be found any pedunculated outgrowth into the floor of the bladder in patients whose hard and fibrous prostates suit them for this operation.

When as much of the gland as seems advisable has been removed, and it is evident that the vesical orifice of the urethra is as low as the lowest part of the bladder, a fair-sized rubber tube is passed into the bladder through the perineum, for drainage, being stitched to the skin, and is gently packed around with iodoform gauze. If the oozing of blood be considerable and cannot be controlled by douching with hot solutions, this packing may be quite firmly applied and remain in place for three or four days. A light gauze dressing, held in place by absorbent cotton and a T-bandage, completes the operation.

On being returned to bed, the perineal drainage is attached by another tube to a bottle hanging beside the bed. The outer dressings may be changed once or oftener daily, as required; the packing should be removed about the fourth day, and the perineal tube at the end of a week. Commencing in the second week, a full-sized catheter or sound should be passed through the urethra every third or fourth day. It will commonly be found that before the end of the second week the patient will pass more urine by the urethra than through the perineal wound. He should be kept quietly in bed until the urine ceases to pass by the perineum. To encourage the voluntary passage of urine, he may turn on his side, or even into the prone position early in the second week.

Suprapubic Prostatectomy. My own technique for this operation does not differ materially from that described by Mr. Freyer.

The patient being in the Trendelenburg position and having not more than 4 ounces of fluid in his bladder, this organ is opened by a suprapubic incision of about four inches in length. The margins of the vesical wound are then to be secured to the abdominal wall by a suture of silkworm-gut on each side. These sutures should pass through the whole thickness of the abdominal wall, and may be either tied and left at the conclusion of the operation, or caught in hæmostatic forceps and removed before dressing the wound. The former plan, which makes a ventrosuspension of the bladder, is not without its subsequent advantages.

By thus securing the bladder to the abdominal wall before the enucleation of the prostate is begun, we both steady this latter organ and render urinary extravasation between the layers of the abdomen exceedingly unlikely.

A rubber catheter is then introduced into the bladder through the urethra, and an incision of an inch or less in length, parallel to the urethra is made in the mucous membrane over the most prominent portion of the prostate as it projects into the bladder. A pair of scissors is safer than a knife for this purpose. The index finger of the surgeon is then introduced into this cut and readily finds a

natural plane of cleavage of the prostate from its sheath. The index and middle fingers of the other hand, gloved, are introduced into the rectum, and with the thumb making counterpressure as well from the perineum, the prostate can be enucleated in a surprisingly short space of time, and with unexpected ease. The vesical orifice of the urethra has in my operations generally torn loose from the bladder wall, and the prostate has come away from around it as a glove is stripped off the finger, leaving the proximal inch of the urethra, formerly embedded in prostatic tissue, lying free in the bladder and only attached where it pierces the posterior layer of the triangular ligament to become the membranous urethra. I have removed the entire prostatic urethra in some of the cases, from which there have been no untoward results; in fact, I believe that it is the rule for the prostatic urethra to be removed with the prostate. The lobe first attacked should be separated from its attachments first posteriorly, then on the outer side and below, and, finally, from the triangular ligament at its apex. If the gland be not too large, both lobes can be freed and delivered through one incision; but if it be of unusual size, it will be found advisable to repeat this procedure for the second lobe through another incision, whereupon each lobe may be delivered separately into the bladder. During these manipulations the original incision in the mucous membrane is, of course, torn larger by the finger.

By clinging close to the capsule of the gland, or even by passing between its outermost planes of tissue (as is claimed by some is always done in this operation), the prostatic plexus of veins is not injured, and there is comparatively little hemorrhage. If the veins are laid bare, it is evident that the whole capsule has been removed; but if a smooth-walled cavity is left behind, the surgeon's finger has, in all probability, split the prostatic capsule, and leaves a layer of this tissue in place. It makes no difference to the success of the operation which has occurred, except that in the former instance some of the veins might be ruptured and cause troublesome hemorrhage. Especially apt is this to be the case where the prostate is the seat of a fibrous rather than a glandular enlargement, or where periprostatitis has existed.

When the surgeon has removed the prostate he will be very much surprised, as well as pleased, to see with what rapidity the cavity from which it has been enucleated contracts. This occurs largely from the pressure of neighboring structures and from the natural elasticity of the parts, and is an event which diminishes the bleeding. Free douching of the bladder with hot saline solution, which both cleanses and checks the unavoidable oozing, together with the introduction of a suprapubic tube, completes the operation, which usually, from beginning to end, lasts not more than thirty minutes. The suprapubic wound may be sutured, except where the half-inch rubber drainage-tube emerges, this being stitched to the skin, and

is dressed with plenty of gauze and absorbent cotton, into which the tube discharges. A catheter is not retained in the urethra, nor do I drain through the perineum. It is sufficient to pass a rubber catheter by the urethra once in every twenty-four hours after the first day or two and to douche the bladder through it, allowing the fluid to drain by the suprapubic wound; recently, however, it is not my practise to wash the bladder out, except through the suprapubic wound.

After forty-eight hours the suprapubic tube may be removed and the patient encouraged to pass his urine. Voluntary micturition commonly returns earlier after this operation than after that by the perineal route; and, as there is no fear of a sinus persisting below, the patient may be propped up in bed on the fourth or fifth day, and be allowed to sit in a chair at the end of a week or ten days if his general health permits.

In both these operations the power of procreation is, of course, destroyed by the unavoidable injury to the ejaculatory ducts; but, as it is questionable whether the spermatic fluid would be ejected without the contraction of the prostate, and as it is probable that it would not be fertile without the secretion of the prostate, the destruction of these ducts is a secondary consideration. The power of intercourse is less apt to be impaired after a suprapubic enucleation than after a perineal prostatectomy, and in some patients in whom it has been lost prior to operation, this procedure appears to have restored it.

A brief report of the cases, 13 in number, in which I have had to resort to Freyer's operation, is appended.

I wish to take this opportunity of crediting my friend, Dr. Astley P. C. Ashhurst, with much of the work done upon this paper, and in particular with the bibliography.

All of these cases were under my care in the German Hospital:

Case I.—T. F., aged sixty-three years; admitted July 30, 1903; discharged September 7, 1903; recovered. Present trouble began in May, 1902. Patient had pain upon urination, had trouble in starting the stream, then a sudden stoppage of the stream. At this time he passed two small stones, some blood, but no blood lately. Passes urine quite often, and at night some eight to ten times. Patient says that when he is up and about he has a feeling that there is a foreign body in the bladder.

July 31, 1903, a stone was detected by means of passing a sound into the bladder.

August 3, 1903. Operation: Three stones removed from the bladder, diameter of a penny and about three-eighths of an inch in thickness. Prostate enucleated.

Case II.—L. F. (No. 1533), aged sixty-eight years; admitted June 30, 1903; discharged September 11, 1903; recovered. No venereal

history. Bowels are regular. Moderate user of tobacco; no alcohol. One week ago infection of middle finger of left hand. For the past two years patient has had trouble in passing his urine, often obliged to get up eight and ten times at night. Some burning upon urination and difficulty in starting the flow. Four days ago inability to pass urine; catheter passed with great difficulty.

On admission 600 c.c. of bloody urine withdrawn; a false passage was detected in passing the catheter.

Rectal examination shows an enlarged prostate quite firm to the touch.

Operation, July 6, 1903: suprapubic prostatectomy.

Fig. 1.

Case III. T. C., aged seventy-seven years. Reduced one-fifth.

Case III.—T. C. (No. 1623), aged seventy-seven years; admitted September 19, 1903. Patient had been suffering from frequency of urination for years, more marked at night. Ten days ago urination became difficult; three days before admission impossible. He was catheterized by a physician for two days with difficulty. Third day catheterization was impossible (Fig. 1).

On admission, bladder greatly distended, reaching to the umbilicus. Prostatic catheter passed; several strictures encountered anteriorly; at the prostatic urethra is a large, false passage leading to the left.

Prostate greatly hypertrophied, the size of a small orange. Urine obtained by catheterization very bloody.

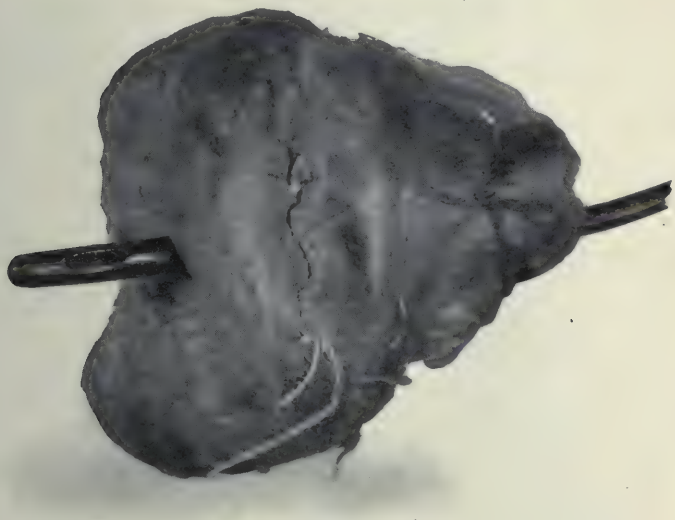
September 21, 1903. English catheter passed, permanently fixed in bladder.

Operation, September 23, 1903: suprapubic prostatectomy. Patient never rallied after operation.

CASE IV.—J. M. C. (No. 1555), aged sixty-three years; admitted July 18, 1903; discharged August 14, 1903; recovered. Patient uses alcohol moderately; tobacco to excess (Fig. 2).

Six months before admission patient first noticed difficulty in starting the stream, especially in the morning; as a rule, was com-

FIG. 2.



CASE IV. J. M. C., aged sixty-three years. Reduced one-fifth.

pelled to urinate once during the night; during the day passed urine about four or five times. Amount said to be scanty; slight pain on starting.

One week before admission was exposed to cold and rain and suffered retention; was relieved by catheter, and since then has been catheterized twice a day.

Rectal examination reveals a firm mass at the neck of the bladder, about the size of a large hen's egg. Amount of residual urine, 50 c.c.

Operation: suprapubic prostatectomy.

CASE V.—D. D. (No. 1469), aged fifty-eight years; admitted May 4, 1903; discharged June 3, 1903. Bowels are regular. Patient uses

alcohol and tobacco moderately; complains of a burning sensation after urination; about one month before admission had to urinate every ten minutes, passing 10 c.c. to 15 c.c. at a time; the stream would suddenly stop and then start up again. Urine highly colored, red, supposed to be bloody. Pain more marked on moving about.

Used to have to urinate every twenty minutes during the night; of late has not urinated so often; three or four times. Pain starts just above the symphysis pubis and shoots down the penis: stinging sensation at end of penis (Fig. 3).

Operation: suprapubic prostatectomy; recovery.

FIG. 3.

CASE V. D. D., aged fifty-eight years. Reduced one-fifth.

CASE VI.—S. L. T. (No. 1542), aged seventy-three years; admitted July 9, 1903. Patient has never used alcohol. Had an attack of gonorrhœa when about eighteen years of age Present illness began about two and a half years before admission, with frequency of urination, especially at night; obliged to get up about every fifteen or twenty minutes to urinate; often when upon his feet he would involuntarily urinate. Flow lacked force, coming in a thin stream; of late bright blood was present. At the beginning of the illness much sediment present in the urine.

Rectal examination shows an enlarged prostate, very firm, size of a lemon (Figs. 4, 5 and 6).

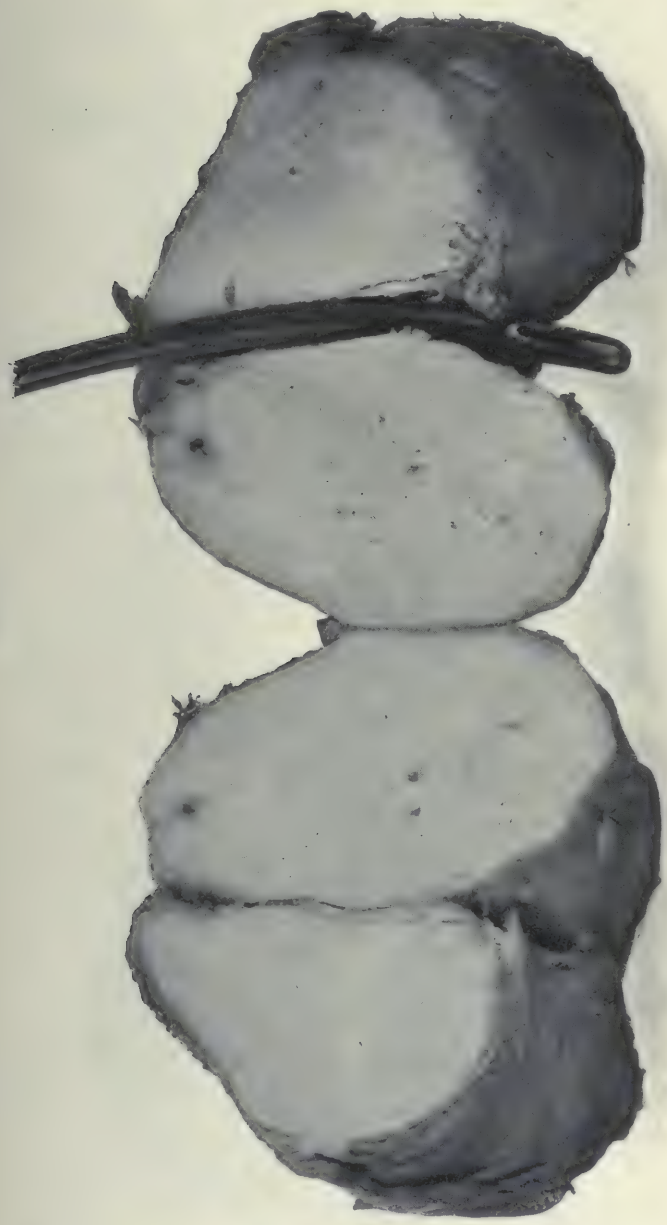


FIG. 4.

CASE VI. S. L. T., aged seventy-three years. Reduced one-fifth.

Operation: July 11, 1903: suprapubic prostatectomy. Patient died July 26, 1903.

Fig. 5.

Case VI. S. L. T., aged seventy-three years. Upper surface. Reduced one-quarter.

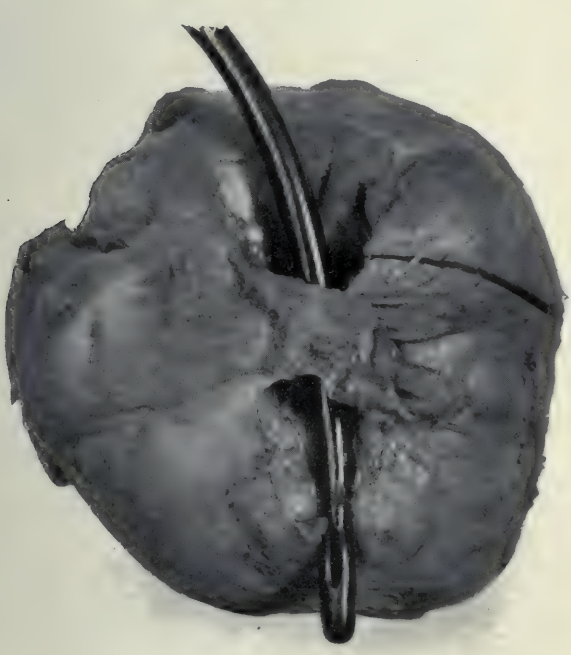
Fig. 6.

Case VI. S. L. T., aged seventy-three years. Under surface. Reduced one-quarter.

CASE VII.—H. M. Y. (No. 1502), aged sixty-six years; admitted June 8, 1903; discharged August 1, 1903. The patient's father died of prostatic disease; a moderate user of alcohol. For past fifteen years had had frequency of urination; most marked at night. Two years before admission suffered from an acute attack of cystitis. In July, 1902, was operated upon for vesical calculus, since which time he has had a suprapubic fistula. Has not passed urine through urethra for six months.

Rectal examination shows very hard prostate, size of a lemon (Fig. 7).

FIG. 7.



CASE VII. H. M. T., aged sixty-six years. Reduced one-quarter.

Operation, June 15, 1903; a stone the size of a lima-bean extracted from the bladder; prostate enucleated; recovered.

CASE VIII.—D. R.; admitted December 9, 1901. For the last eight years patient has been troubled with dribbling of urine; for two years had had overflow of retention due to an hypertrophied prostate.

Rectal examination shows prostate size of a small orange; bilateral enlargement.

Operation: suprapubic prostatectomy. Patient died of uræmia, December 23, 1903.

CASE IX.—J. S.; admitted February 24, 1901; discharged April 5, 1901. Seven years before admission patient began to have frequent and painful urination; pain would shoot to penis and groin. Was operated two years later for stone in the bladder; both testicles became involved and were removed. Had had a perineal section done, in which part of the prostate gland was removed one year before the stone was removed. Gradual atrophy of penis. Ever since stone was crushed he had had cystitis. Urinated eight to ten times during the night and every hour in the day. Prostate hard; not enlarged.

Operation: suprapubic prostatectomy; recovered.

CASE X.—J. J. M., aged sixty-nine years; admitted September 14, 1903; discharged October 15, 1903. Six years before admission patient began to have "bladder trouble," frequent urination; for two years had used a catheter; now every two hours, with much pain.

Urine very cloudy and ammoniacal odor. By rectal examination a large soft prostate can be felt.

Operation: suprapubic prostatectomy; recovered.

CASE XI.—J. S., aged fifty-six years; admitted March 19, 1903; discharged May 9, 1903. Patient uses alcohol moderately; had chewed and smoked to excess until within ten years before admission. No venereal history. Bowels regular. Four years before admission patient noticed trouble in micturition, slowness in starting the stream, frequency of urination at night; no pain. Used catheter three to five times daily for three years. Has no difficulty in passing catheter, and when introduced expulsion from the bladder seems unimpaired.

Rectal examination reveals enlarged prostate, moderately firm, extending posteriorly into the bladder.

Operation: suprapubic prostatectomy; recovered.

CASE XII.—A. S. (No. 1826), aged sixty-eight years; admitted March 25, 1904. Patient always enjoyed good health, lived a very active life.

Present History. Had frequency of urination fourteen months prior to admission to hospital, during which time he had used a catheter as often as every fifteen minutes. Residual urine not noted.

Has been confined to bed for the last three months with continuous catheterization (Figs. 8 and 9).

March 26th. Operation: suprapubic prostatectomy. Suprapubic drainage with half-inch rubber tube. Urine from bladder through drainage-tube clear.

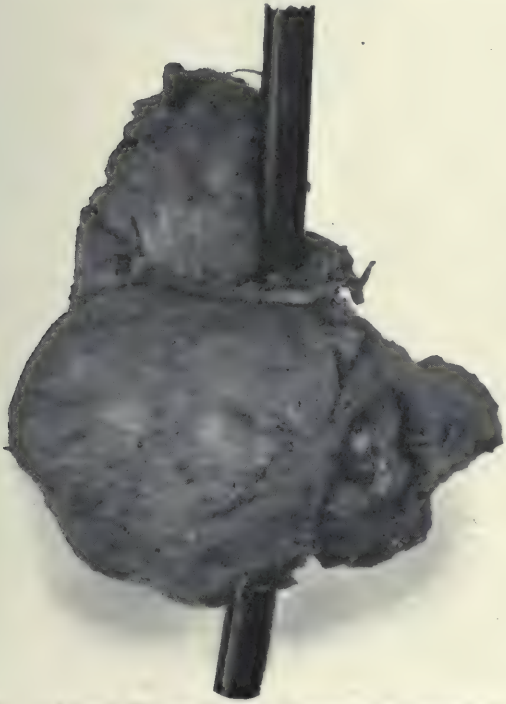
29th. Tube removed. Drainage from suprapubic wound without tube.

April 6th. Voided small amount of urine by urethra. Patient still under treatment.

Fig. 8.

Case XII. A. S., aged sixty-eight years. Under surface. Reduced one- fifth.

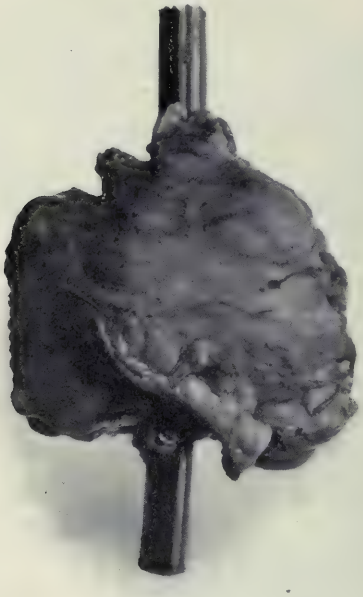
Fig. 9.



Case XII. A. S., aged fifty-eight years. Upper surface. Reduced one-fifth.

CASE XIII.—P. J. (No. 1810), aged sixty-five years; admitted March 5, 1904. Patient has had frequent urination day and night for some time. Four weeks before admission patient was unable to pass urine; since then he has had to be catheterized, twice a day at first, lately three times a day. By rectal examination prostate is found enlarged. Residual urine 300 c.c. (Fig. 10).

FIG. 10.



CASE XIII. P. J., aged sixty-five years.

March 12th. Meatotomy.

20th. Suprapubic prostatectomy, suprapubic drainage by rubber tube.

23d. Urine by tube clear.

24th. Tube taken out.

25th. Small amount of urine passed through urethra. Patient still under treatment.

STATISTICS.

Suprapubic permanent drainage.

Operator.	Cases.	Deaths.	
McGuire	39	2	
Poncet	35	0	
Horwitz	33	0	
	107	2	Mortality 1.87 %

Bottini operation.

Operator.	Cases.	Deaths.	
Bangs	42	3	
Horwitz	33	0	
Meyer	59	7	
Young	41	3	
	175	13	Mortality 7.5 %

(Freudenberg, in 1900, collected 753 operations by Bottini's method, 44 of which, or 5.8 %, terminated fatally.)

Perineal prostatectomy.

Operator.	Cases.	Deaths.	
Albarran	35	1	
Deaver	5	2	
Ferguson	6	0	
Horwitz	7	3	
Murphy	8	0	
Syms	9	0	
Verhoogen	3	0	
	73	6	Mortality 8.2 %

Freyer's operation.

Operator.	Cases.	Deaths.	
Barling	10	3	
Freyer	51	5	
McRea	3	0	
Moynihan	12	1	
Stoker	3	0	
	79	9	Mortality 11.3 %

McGill's operation.

Operator.	Cases.	Deaths.	
Armstrong	9	4	
Fuller	5	0	
Horwitz	5	1	
Thorndike	9	1	
	28	6	Mortality 21.4 %

(Belfield, in 1890, collected 88 cases of suprapubic prostatectomy, with 12 deaths, a mortality of 13.6 %; and Moullin, in 1892, collected 94 cases with 19 deaths, or 20.2 % mortality.)

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THE CLINICAL VALUE OF THE AVERAGE ANALYSIS OF GASTRIC CONTENTS.*

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of New York.

I have been led to a consideration of this subject by reading a passage in Hemmeter's[1] book on *Diseases of the Stomach,* in which he says: "It would be a valuable contribution by various gastro-enterologists of the United States if they collected and reported the frequency of hyperacidity and other gastric diseases occurring in their localities, so as to throw light on the influence of race, climate, and geographical distribution," etc., and further, by reading a statement by Riegel,[2] that the determination of the frequency of hyperchlorhydria will remain impossible, so long as every dyspeptic is not examined by lavage, and that hyperchlorhydria is encountered more frequently in private practice than in hospitals, because the symptoms of this condition are generally not severe enough to send the patient to an institution. It is evident that there is much truth in both of these apparently opposite statements, but of the two, the one which appeals to us most in connection with the subject in hand is that of Riegel, for it demands a thorough examination of each case in as scientific and uniform a manner as possible. So long as the various observers in different parts of the country do not employ the same methods and base their conclusions upon uniformly imposed conditions, so long will it be impossible to correctly determine the actual prevailing distribution and frequency of chronic gastric diseases.

We have but to glance at the reports of various observers in different parts of the world to see the force of these statements. If we take hyperchlorhydria as an example, it will be found that, so far as its frequency is concerned, it is reported as follows: by Schneider[3] (Zurich) at 5 per cent., by Kovesi[4] (Budapest) at 30 per cent., by Johnson and Böhm[5] (Stockholm) at 36 per cent., by Jaworski[6] (Lemberg) at 50 per cent., of all chronic gastric diseases; by Mathien, Bouveret, and Renaud, as exceedingly frequent in France; by various American authorities at about 50 per cent. of all stomach cases; and by Fleiner[7] (Heidelberg) and Westphalen[8] (St. Petersburg) as comparatively rare.

There can be no doubt that the different results which come to us from Continental observers may be due, in part, to differences in nationality, temperament, class conditions, and especially food, but it is also probable that they are due to non-uniform methods of

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examination, and a divergence of the imposed conditions for judging this complaint. This latter fact is especially pertinent to this country, for differences of nationality and temperament are, to a certain extent, blended here by social conditions, customs, and intermarriage; but, what is more important still, is the fact that economic conditions are such that differences in diet due to class distinctions do not operate to the same extent as they do on the Continent. We have no potato-eating Irish peasantry or rice-eating Japanese peasantry as national factors. The general scale of wages makes it possible for most artisans and laborers to nourish themselves in a proper manner. This is more than evident with ordinary skilled labor at five dollars per day. If, then, there are differences of opinion as to the relative frequency of chronic gastric diseases, we must look for the cause of these in a non-uniformity of methods employed and a diversity of opinions as to the necessary conditions to be imposed upon a patient in order that a correct diagnosis may result.

In this connection, I have chosen the acid secretion of the stomach as the subject for inspection, simply because it is the function about which we know the most and the knowledge of which, after all, so far as the diagnosis of most chronic diseases is concerned, gives us the greatest aid. It is also in the determination of hydrochloric acid that the greatest errors in judgment are made. These errors do not relate to the actual chemical reactions which take place in the test-tube or beaker after the gastric contents have been extracted, but relate to the best possible methods for developing the acid secretion of the stomach for clinical purposes. The simple finding of such and such a quantity of hydrochloric acid at a given time in a given stomach often serves only to mislead. The real object of gastric analysis is to determine the secreting capability of the stomach under the conditions in which it finds itself. This leads to a consideration of the methods which are employed for this purpose.

The whole question resolves itself into this: Can we secure a better knowledge of the gastric-acid secretion by employing carbohydrates or proteids, as exemplified in the ordinary test breakfast of Ewald or the more complicated meat-containing meal of Riegel? Or had we better use both of these meals; or, would it be wiser to discard both of these tests as placing the organ under unnatural conditions, and examine the same under the circumstances in which it finds itself, and containing the food to which the individual has been accustomed, or which has led to his discomfiture?

It would appear at first sight to be rank heresy to make a proposition such as the last, after the years of trial which the first two methods have endured; but it is also evident that there is a certain difference between gastric analysis for scientific purposes and gastric analysis for clinical diagnosis. The proposition is further justified, when we consider that very few people take kindly to tea

without milk or sugar and dry bread, and that in a certain proportion of cases a diagnosis, which remains uncertain under the usual tests, suddenly becomes clear as day if the patient is placed on his natural diet and usual conditions of life.

In order to fully consider the question, it will be necessary to review in brief three separate lines of experiment which have been pursued for years, and which have a direct bearing upon it. They may be called the diagnostic, the dietetic, and the physiological. The first two are closely allied in that they have had for their object the study of the extreme development of the acid secretion of the stomach, and the results which have been obtained in each are directly interchangeable, for that food product which is of greatest service in the development of the acid secretion for diagnostic purposes would necessarily play an important part in the treatment of gastric conditions in which the quantity of acid is found to be abnormal. A study of the question would further be incomplete should we not take into consideration the remarkable results obtained by Pawlaw in the purely physiological line, for these have revealed the marked influence of such special senses as taste, sight, and smell upon the gastric secretions in general—factors of the greatest importance in this connection.

The value for diagnostic purposes of the ordinary trial breakfast of Ewald or the proteid-containing meal of Riegel has been variously estimated by different observers. Ewald, Boas, Leube, and Jurgensen have been the chief defenders of the first, whereas Riegel, Fleiner, Fleischer, and Rosenheim have contended for the latter. The objections to the test breakfast are its simple, non-stimulating character, that it does not appeal to the special senses, and hence does not give an adequate knowledge of the secreting capability of the stomach. On the other hand, its uniform character seems to be the quality which appeals most to those who prefer it. The chief objections to the meat-containing meal have been its non-uniformity of character and the greater difficulty in manipulating it. In this connection, Rosenheim,[9] while admitting the general utility of the test breakfast, says that the meat-containing meal is better suited to scientific purposes. Fleischer[10] contends that the trial breakfast is non-stimulating, and Fleiner[11] regards the use of the two meals as largely dependent upon the habits of the patient. Riegel[12] admits the uniformity of the test breakfast, but says that it gives an insufficient idea of the secreting capability of the stomach, for a stomach may be able to produce free hydrochloric acid with a test breakfast and yet be incapable of doing the same when called upon to digest a general diet containing proteids. Leaving aside considerations of non-uniformity of character or ease of manipulation, the whole subject seems to resolve itself into a discussion of the stimulating properties of carbohydrates and proteids to the gastric secretions, for an ordinary test breakfast, after all, is largely

carbohydrates. (The ordinary wheat of the United States, according to König, contains about 10 per cent. water, 10 per cent. nitrogenous product, 2 per cent. inorganic substances, and the remainder carbohydrates.)

Another phase of the same controversy which has been going on for years relates to the proper dietetic treatment of such abnormal gastric acid conditions as hyperchlorhydria. This was practically begun by von Sohlern,[13] in 1891, after Moritz[14] (1889) and von Jaksch[15] (1890) had declared, from clinical observation, that carbohydrates were less stimulating to the gastric secretions than proteids. Briefly glancing over the various turns in the struggle, we find that von Sohlern placed all his patients upon a carbohydrate diet and was followed in the course of years by Rosenheim, Fleiner, Justesan, and Jurgensen. In 1895 Schüle,[16] after more exact experiments upon normal stomachs, declared the free hydrochloric acid was about the same in both diets, that there was a slight increase of the total acidity in cases where proteids were administered, and that the height of digestion was prolonged in the latter class of cases. In 1897 Jurgensen[17] opposed the view of Schüle by declaring that a proteid diet directly increased the quantity of acid secreted, on account of its greater combining power. In 1898 Sorensen and Mezgar,[18] experimenting upon cases of hyperchlorhydria, expressed the opinion that in this condition the free hydrochloric was about the same in both diets. In the same year Hemmeter[19] advised the use of carbohydrates in hyperchlorhydria, on account of the danger of a greater proliferation of the oxyntic cells than already existed in this condition. In 1899 Schüle[20] admitted that carbohydrates caused less secretion in hyperchlorhydria, but still maintained that the free hydrochloric acid was practically the same in both diets, and that in normal cases there was no great difference between the two.

This variety in the results obtained can only be explained by the diversity of the methods employed and the conditions imposed. In some cases normal stomachs were utilized and in others hyperchlorhydric ones. Some experimenters employed as tests meat and water, others potatoes and water, and still others bread and beef-tea. In 1899 Bachmann,[21] realizing the vagaries of former experiments, attempted to eliminate them by administering his various foodstuffs according to their nutritive values as expressed in heat units liberated by their combustion and considered only the absorbable portion of the products in his calculations. In short, he determined the quantity of food to be administered according to the isodynamic values of Rubner. These indicate that 100 grams of bread equal 190 grams of beef, or 180 grams of eggs, or 300 grams of potatoes, or 335 grams of oatmeal, or 390 grams of milk. The water contained in each was taken into consideration and proper mixtures made, so that the isodynamic value of each combination was the same.

The experiments were conducted upon previously cleansed normal stomachs, and repeated until the results were constant. The results obtained relate to the free hydrochloric acid, the total hydrochloric acid, the total acidity, the time of maximum secretion, and the duration of digestion. It was found that the first exhibition of free hydrochloric acid takes place for bread in one-half to three-quarters of an hour, for beef in one to one and one-half hours, for potatoes and milk in three-quarters to one hour. Free hydrochloric acid appears one-half an hour earlier in a bread test meal than in an isodynamic one containing beef. Free hydrochloric acid was greatest in case of potatoes and lowest in case of milk and eggs. With a standard for bread taken at 100 the quantity of free hydrochloric acid secreted for beef and potatoes would be 11 per cent. to 21 per cent. plus respectively, and for eggs and milk 14 per cent. to 16 per cent. minus respectively. Such differences existed for simple foods. In cases of more complex diets, that one containing beef showed on the average 12 per cent. more free hydrochloric acid. According to the same standard, the total hydrochloric acid was found to be 5.3 per cent. plus for potatoes, 36.2 per cent. plus for beef, 14.2 per cent. plus for eggs, and 1.3 per cent. plus for milk. In a complex meal containing beef the total hydrochloric acid was 22.5 per cent. plus. The total acidity was 35.5 per cent. higher in a beef-containing meal. The results obtained for the duration of digestion of the various foods was about the same as that given by Penzoldt. From all of which Bachmann concludes that a vegetable diet is indicated in hyperchlorhydria, suggesting that there are two objects of treatment in this condition, namely, the symptoms themselves and the process producing them (*indicatio symptomatica* and *indicatio morbi*). All treatment should be directed to the latter, advice which had already been given by Jurgensen and Hemmeter.

From such experiments, carried on in normal stomachs under exact scientific conditions, it was reasonable to suppose that the question had been more or less definitely settled. Here, however, we again encounter the difficulties which separate the results obtained by scientific experiment and the direct application of the same for clinical purposes. In 1900 Mayer,[22] operating in Boas' laboratory, while admitting the scientific soundness of Bachmann's observations, arrived at the conclusion that before the same could be of practical value, it would be necessary to demonstrate that the prolonged use of a vegetable diet could produce a diminution of the quantity of acid secreted. Experimenting with distinct vegetable and meat diets successively upon the same cases of hyperchlorhydria over extended periods of time, he found that the free hydrochloric acid and the total acidity were increased by the continuous use of vegetables. This peculiarity Mayer ascribes to the necessary increased bulk of a vegetable diet and the consequent increased mechanical irritation of the mucous membrane. On the other hand, the con-

tinuous use of proteids in this condition can only be looked upon as a palliative measure, in so far as such a diet has a greater combining power.

Nothing can demonstrate the soundness of these views better than the experience of actual practice. Aside from the utter impossibility of feeding patients for any length of time upon distinct carbohydrate or proteid foods, the results obtained thereby do not justify the means, for, notwithstanding the possibility of increasing or diminishing the demands made upon the average stomach by regulating the diet in one direction or the other, it will usually be found that in the great majority of cases the tendency to secrete too much or too little acid will persist even though all actual symptoms of the disease have disappeared. I have repeatedly examined at long intervals the gastric contents of patients who had suffered for years either from increased or diminished acidity and who had apparently recovered the entire use of the organ, judging from their general comfort and good physical condition, only to find that the same abnormalities of secretion continued to exist. This is most forcibly illustrated in a half-dozen cases of gastroenterotomy in which it was possible to make yearly complete physical and chemical examinations, and which exhibited no changes in their secretory conditions at the end of four, five, and six years, notwithstanding the fact that the causes for the original abnormal secretion of acid had been removed by operation. The importance of this tendency is being realized more and more yearly, and the growing feeling, judging from the most recent literature, is to place patients afflicted with abnormal gastric acid secretions upon plain, bland, and nutritious diets, with less consideration shown for their actual chemical composition than for their unirritating physical properties.

It may appear at first sight to have been superfluous to enter into this review of treatment in a discussion which only involves diagnosis, but as our methods for the development of the acid secretion of the stomach are mainly dietetic, it has seemed necessary to do this in order to have a comprehensive view of the whole subject, for it sometimes happens that the differential diagnosis of obscure gastric affections must depend upon differential treatment. The differentiation between gastric ulcer with hyperchlorhydria and simple gastralgia with hyperchlorhydria can often only be made in this way. If further there exists doubt as to the proper dietetic treatment of abnormal acid conditions in the stomach, there must also exist doubt as to the best method for diagnosing them.

In every case of chronic gastric disease involving abnormal acid secretion, the object of examination is to develop, if possible, the average capability of the stomach to secrete acid and to discover any vagaries of the same which may exist. In order to do this intelligently it would appear to be necessary to place the stomach under its most natural conditions. Can we do this by giving simple

tea and dry bread? A partial solution of this problem is found in the results obtained by Pawlaw[23] by physiological experiments conducted to show the influence of real and fictitious feeding. Briefly tabulated for the purpose of reference, these would be the following: 1. The centres for gastric secretion are located in the stomach wall (splanchnic section causes no cessation of secretion). 2. The vagi serve as transmitters of mental impressions, such as appetite and control secretion in an inhibitory manner (section of the nerves causes hypersecretion during the first few weeks after operation). 3. The quantity of gastric secretion stands in direct relation to the quantity of food introduced. 4. The secretion of acid is continuous during digestion, begins four to five minutes after the introduction of food, and gradually rises and falls to and from the height of digestion. 5. Each particular food has its special acid curve, the summit of which is reached most rapidly in a meat diet. 6. Simple mechanical irritation of the gastric mucosa produces no acid secretion.

The principal impression conveyed by these results, so far as diagnosis is concerned, is that any food test for the development of the gastric acid secretion which is to give satisfactory data for judging the average functional capability of the stomach must not only appeal to appetite, inducing special senses of sight, taste, and smell, but must also be a direct stimulant to the secretory centres in the stomach wall, for Pawlaw has demonstrated that the acid secreted during the first half-hour of digestion is due to the first, and that the real contact stimulation begins later. In the words of Troller, the test must be a physiological stimulant and a physical-chemical stimulant. An interesting experiment is recorded by Pawlaw in this connection. By feeding a dog 200 grams of food he secured 135 c.c. of gastric juice. By directly introducing the same quantity of food into the stomach through a fistula he secured 50 c.c. of gastric juice (sympathetic stimulation). By fictitious feeding of the food he secured 75 c.c. of gastric juice (vagus stimulation). The sum of the last two quantities would be 125 c.c., or pretty nearly the quantity obtained by feeding the animal in the natural way. Pawlaw found further that the introduction of simple substances, such as dry bread, starch, peptone, or egg albumen into the stomach, produced very little secretion. If, however, they were masticated first they caused some secretion. Troller also found that the introduction of food into the stomach through a stomach tube in the human subject produced much less acid secretion than if the same were first masticated. On the other hand, the mastication of tasteless substances caused very little acid secretion.

If we accept these results obtained by clinicians and physiologists —and there is no reason up to the present why we should not—the ordinary trial breakfast does not fulfil the requirements of a physiological test for the acid secretion. It fails in three ways: It fails

to excite the appetite, and hence the vagus stimulation in those cases in which it is taken with repugnance. It fails to be a physical-chemical stimulant because it does not act as an energetic stimulant to the secretory centres. It fails because it places the individual in an unnatural condition of life for examination. Hence it cannot be surprising that this meal should give a variety of results in clinical work, results which in a good proportion of cases are erroneous, or, stated in a more conservative manner, results which may be correct for tea and bread, but erroneous for the average normal diet of the individual.

In order to demonstrate this, I have taken statistics from some hundreds of cases of my records by comparing the results obtained from successive analyses in the same cases. Among women, three-quarters to one hour after a trial breakfast, I found 60 per cent. were hypochlorhydric, 30 per cent. normal, and the remainder hyperchlorhydric. Upon the next examination I found that 57 per cent. had remained stationary, whereas 43 per cent. had changed as follows: of the subacid cases, 22 per cent. became normal and 2 per cent. hyperacid; of the normal cases, 14 per cent. became subacid; and of the hyperchlorhydric cases, 2 per cent. became normal. Among men the changes were not so marked. Of these cases, 43 per cent. were subacid, 35 per cent. were normal, and 22 per cent. hyperchlorhydric. Upon the next examination 72 per cent. remained stationary and 28 per cent. changed as follows: of the subacid cases, 10 per cent. changed to normal; of the normal cases, 4 per cent. changed to subacidity and 6 per cent. to hyperchlorhydria; of the hyperchlorhydric cases, 12 per cent. changed to normal and sometimes to subacidity. Taken collectively, men and women, it was found that 60 per cent. remained stationary and 40 per cent. had changed upon successive examinations.

This variation cannot be due to the uncertainty usually attached to first examinations. These were carefully excluded, as I have come to the conclusion that first examinations generally give false results. This is due to misunderstanding in regard to quantity and quality of the food to be taken, duration of digestion, and such emotional disturbances as anxiety, uncertainty, and fear. Upon the second examination these objections are largely removed. Nor can the variation be attributed to nervous dyspepsia, for such cases were excluded from the list. There remains but the one conclusion that the differences in results are due to something inherent in the test itself. This is not surprising when we recall the results obtained by Pawlaw. The average patient approaches plain tea and dry bread with disgust and annoyance. It does not appeal to his appetite through the special senses, and yet nearly one-half of the gastric secretion is induced through them. In this connection, we have the interesting observation, made by Pawlaw, Bachmann, and Buch, that the addition of a little butter to the bread, thus rendering it more

palatable, will often materially increase the quantity of acid secreted, though fats are supposed to inhibit the acid secretion. That this appeal to the appetite of the individual is of paramount importance is best illustrated in the one-time manufacture of commercial pepsin, when pigs were placed within sight and smell, but out of reach, of enticing food, only to be slaughtered after a length of time sufficient to allow the peptic glands to become filled had elapsed.

It will be asked why the ordinary test breakfast, which is so slightly stimulating, should produce hyperchlorhydria in any case. The anomaly can be explained in various ways. In some of these cases the increased acidity is only momentary, and is due to emotional disturbances, for such may induce either hypochlorhydria or hyperchlorhydria in stomachs which, as a rule, are perfectly normal. In other cases the abnormality is due to defective innervation of the stomach itself, in so far as the gastric secretion does not adapt itself to demands made upon the organ. In other cases, still, the hyperchlorhydria may be due to proliferation of the oxyntic cells, so that the introduction of any food substance into the stomach would probably cause an increased acidity. In the first two classes of cases the administration of a more palatable diet will cause the hyperchlorhydria to disappear. In the last class such administration will cause a still higher acidity, in that the secretion of acid is directly proportional to demand as in normal stomachs, the only difference being that in hyperchlorhydric cases there is an increase of gastric secreting cells. It is not always possible to demonstrate this by estimating the free hydrochloric acid alone, as the total hydrochloric acid may be increased markedly without there being any evidence of this in the quantity of free hydrochloric acid present. This latter quantity may fluctuate to a certain extent in the case of more complex diets. This is due not only to the combining power of the administered food, but also to the muscular activity of the gastric walls to secure a thorough admixture of the food and the acid secreted; and, further, to the intensity of the chemical reactions which takes place in the stomach, for from recent experiment there is some evidence that the combination of hydrochloric acid and proteid within the stomach need not be permanent, but that part of the acid may be released from the acid-proteid molecule to begin anew the attack upon other proteid molecules.

It is not necessary to conclude from these observations that the ordinary test breakfast has lost its usefulness. On the contrary, as a preliminary and comparative test, it is invaluable, for any stomach which will secrete too much acid with this test may be said to have something wrong either in its innervation or its secreting structures. In order to determine the causes of abnormal secretions produced by this method, it would be advisable to compare the results obtained by it with those obtained by other methods from which some of its objectionable features have been removed; in other

words, some test which will appeal more to the patient and which will be more normally physiological in its action.

Some of the objections to the test breakfast can be removed by the addition of proteids of some kind, as typified in the meal of Riegel. Such addition would serve several purposes. It would render the test more acceptable to the patient in that its preparation would enhance its savor. The results obtained would roughly indicate the difference between carbohydrate and proteid stimulation. In cases of subacidity after a simple test meal the increased stimulating quality of the proteid may produce a normal quantity of acid, showing that the membrane is still in condition to furnish sufficient acid for digestive purposes. Finally, in some cases of hyperchlorhydria after a test breakfast, due to the exotic nature of the latter, proteids may again produce normal results. In many cases deceiving extremes would be curtailed, and we should expect more uniform results. In order to accomplish these ends in the simplest possible manner, it has been my custom to employ a meal composed of the ordinary test breakfast, with the addition of one-quarter of a pound of lean, finely chopped beef prepared by broiling and slight seasoning to render it palatable. This meal is usually taken with relish, is easily extracted from the stomach, and filters as readily as an ordinary test meal. It is examined three hours after it is taken.

Operating in this manner upon a long series of cases, 40 per cent. were found to be subacid, 46 per cent. normal, and 14 per cent. hyperchlorhydric. Upon further examinations, 35 per cent. remained subacid, 54 per cent. remained normal, and 11 per cent. hyperchlorhydric. Compared with the results obtained after trial breakfasts, the number of subacidities was reduced 23 per cent., the normal cases increased 15 per cent., and the hyperacid cases increased 9 per cent. This would indicate that the results after the proteid-containing meal are not only more constant, but also that the frequency of the various conditions is changed, the general tendency being to bring the extremes of secretion to the normal standard. This is perhaps best illustrated in a series of cases in which both meals were employed. In these cases after several examinations the free hydrochloric acid remained stationary in 67 per cent. In 33 per cent. the free hydrochloric acid after trial breakfasts was diminished in 18 per cent. and increased 15 per cent. after proteid meals. Of the subacidities after the trial breakfast, 70 per cent. remained stationary and 30 per cent. advanced to normal after the proteid meal. In the same manner 27 per cent. of the normal cases became subacid and 64 per cent. remained stationary, judging from the free hydrochloric acid alone; 38 per cent. of the hyperchlorhydric cases became normal after proteids. In 20 per cent. of the cases anachlorhydria prevailed throughout.

Whatever these results may be worth, they at least illustrate that

a palatable proteid-containing test will often prevent errors in the judgment of the secreting power of the stomach by appealing to both sources of gastric secretion and by placing the stomach under more natural conditions. It has been my experience to find that, while on the one hand the repair of the secretory functions of the stomach when once damaged is exceedingly slow and generally impossible; so, on the other hand, the impairment of the same functions is slow also, and that many stomachs which under the ordinary clinical tests do not secrete properly, will do so provided they are given an opportunity. In tempting a stomach to secrete with simple tea and bread, we are only replacing the starvation diet, to which most chronic dyspeptics have long subjected themselves by a starvation test, and it is known to everyone what a liberal change in this direction will often do for a great many of these patients.

Aside from these advantages derived from the systematic and successive administration of these two tests for judging the capability of the stomach to secrete, there is another which should not be neglected. This relates to the possibility to suspect the pathological processes which have taken place in the secretory structures by an analytical comparison of the various results obtained by the two methods. If a stomach which is persistently subacid after trial breakfasts becomes normal after proteids, we may safely conclude that the secretory structures are normal. Without the proteid test the subacid condition may just as well have been attributed to a neurosis (provided always that there were not other signs of structural changes), for there had been no sufficient demand made upon the organ by the simple tea and bread. With such results one would also be justified in suspecting an atonic condition, in that the continuous presence of food had rendered the organ less sensitive to slight stimulation. If, on the other hand, the subacid condition remains stationary after both tests, it is quite probable that organic changes have occurred, for the increased stimulation of the proteid should have produced more acid, even in cases where a neurotic element exists. In those cases in which a subacidity after trial breakfasts suddenly develops into a hyperchlorhydria after proteids, there is fair evidence that a condition of defective innervation may be present, for were the cause of the marked difference to be found in a proliferation of the gastric cells in the sense of Hemmeter, Einhorn, and Cohnheim, we should, at least, have had normal acidity, with such slight stimulation as tea and bread affords. The same condition of defective innervation may be suspected in those cases of hyperchlorhydria after a trial breakfast which become normal after proteid meals, for there is nothing in the stimulating property of a trial breakfast to call for the increased acid secretion. If, however, a hyperchlorhydria after a trial breakfast persists or increases after proteids, we have good reason to judge the case one where proliferative changes have taken place in the mucous

membrane, for the secretion of acid has been directly proportional to stimulating properties of the food. This is especially the case if the symptoms of hyperchlorhydria occurs several hours after meals, showing that the secretion of the acid has been progressive and not regular. If, on the other hand, the symptoms and the production of increased acidity occur directly after meals and gradually disappear as digestion progresses, we may again suspect defective innervation. In these cases the secretion of acid is irregular, in that the mere presence of food is sufficient to cause a very rapid secretion of acid not regulated by demand and which soon exhausts itself through its own energy. Hence, both symptoms and hyperchlorhydria disappear during the later stages of digestion. That such rapid production of fluid, acid or neutral, may take place in the stomach is best demonstrated by those cases of nervous dyspepsia in which sudden and voluminous regurgitation of fluid occurs in individuals who have taken no fluids for some time previous and whose stomachs are not atonic.

I have given these few examples to demonstrate the possibility for analytical deduction from the results obtained by the determination of the acid gastric secretion. The mere presence of so much acid in a stomach at a given time is not sufficient to establish the digestive capability of the organ, and the older practitioners are justified, to a certain extent, when they look with distrust upon gastric analysis in general. Unless the average capability of the stomach to secrete is developed by a systematic course of examinations in some such manner as given, it would be far better to depend for diagnosis and treatment upon clinical observation and a good history. It is manifestly impossible to demonstrate the secreting power of a stomach by giving one meal or one kind of meal. It would be just as reasonable to expect a dog to secrete natural gastric juice by feeding him flour paste through a tube or by going into the rice fields of Japan to hope to secure an idea of the natural gastric secretion of the peasants by giving them test meals of unsavory and unseasoned plain meat and tea. In the one case proteids are required, in the other carbohydrates. In this country, and in our larger cities especially, people are accustomed to mixed diets, and highly seasoned ones at that; so that the administration of simple food tests will often not suffice to reveal the average natural secretion of the stomach. In order to do this properly more complicated measures are necessary, the rules for which have already been given in the clinical and physiological studies of Bachmann and Pawlaw, by directing us to begin with simple tests, and then gradually to lead up to more complicated ones by adding palatable proteids, etc. By a comparison of the results obtained, we will generally be able to secure a good idea of the average capability of the stomach to digest. At least, we will know how it acts under mild and strong stimulation. Practically this can be accomplished by giving simple tea and bread

tests at first and later adding to this same test a simple proteid, such as a quarter of a pound of finely chopped lean beef palatably but simply prepared by broiling and slight seasoning. Two each of these meals should be given upon fasting stomachs upon successive days.

It will sometimes happen, however, that with all possible care as to such systematic examination, we are unable to secure an adequate idea of the secreting capability of some particular stomach in its relation to given symptoms. The reason for this would seem to lie in the very nature of the conditions imposed. Scientific and exact they may be, but they are also more or less unnatural, and in certain individuals of sensitive temperament they may defeat the very object for which they were intended. In a certain proportion of chronic gastric cases, starvation tactics have been employed to such an extent that not only does the stomach not do its work properly, but all the organs are more or less dilatory in their action. In such cases it is advisable at times to feed the patient generously, but plainly, for a few days, and then examine the gastric contents three hours after a plain but appetite-inducing mixed meal. It is remarkable to what extent this simple procedure will often aid in diagnosis by giving results which are quite different from those obtained by previous methods. It may be that the dyspeptic symptoms will be temporarily aggravated by this method, but there is a certain advantage in this also, for the nature of some forms of chronic gastric disease with remittent symptoms can often only be elicited by examination during the period of suffering. At this time any vagaries or abnormalities of secretion are exaggerated to such a degree as to make it possible to detect them easily, whereas the same may be masked in the interval. I can recall several cases of individuals in whom repeated gastric examinations revealed normal secretion, but who would occasionally be taken with very severe pain in the stomach accompanied by excessive gas formation and acid eructation. Examination at this time would show intense hyperchlorhydria with food retention. As the stomachs were perfectly normal in the intervals and the attacks would occur without indiscretions of any kind, in the midst of perfect health, it was difficult to understand the cause for a long time. Close observation, however, revealed that sudden atmospheric changes would bring on the attacks. Whether the primary condition was the hyperchlorhydria, with secondary pyloric spasm and retention or *vice versa*, it would be difficult to say. Judging from the suddenness of onset and the rapidity of development of the attacks, it would appear that a pyloric spasm was the causative factor. In none of these individuals could a general neurosis be demonstrated.

The advantage, for diagnostic purposes, of the existence of pronounced symptoms at the time of examination is further demonstrated in certain other forms of chronic gastric diseases with remittent symptoms. I refer especially to conditions of occasional periodic

atony in neurotic individuals. Cases of acute indigestion with retention due to indiscretions are not included in this category. The cases referred to are only those in which a temporary atonic condition is developed as a result of intense mental and physical depression, so commonly encountered in general neuroses. That such a localized muscular weakness in the stomach should accompany the general depression is natural, and the same disappears as the general condition improves. The duration of these temporary atonic conditions may be anywhere from twenty-four hours to days, and they are probably due to temporary loss of excitability in the ganglionic centres controlling the muscular action of the whole alimentary tract. Hence, they are not atonic conditions in the usual sense of the term, for there is no inherent disability in the muscular fibres themselves. Examined during these spells, such a stomach will contain food at a time when it should normally have been empty, and the diagnosis of atony is made, especially if a little sagging is present at the same time. Lavage is ordered, tonics are given, the diet scrupulously regulated, and the patient improves remarkably, whereas a second examination at the end of twenty-four or forty-eight hours would probably have revealed a perfectly normal stomach. Here, again, is demonstrated the necessity for repeated physical examinations in order to determine the average muscular activity of the stomach, for it is quite certain that vagaries may exist in this function also.

It has not been my object in presenting this subject to suggest improvement in the technique of gastric analysis, nor have I intended to convey the impression that the determination of the acid secretion of the stomach is the factor of paramount importance in diagnosis. This one function was selected simply because it was possible by it to judge the value of gastric analysis in general in the light of physiological research. Everyone knows that a proper knowledge of the other function is quite as important, and that all facts, whether they be elicited by chemical analysis, physical examination, or the etiology, must be carefully considered in each case. It is well known further that a correct diagnosis can be made in many instances without any gastric analysis whatever. It seems to me, however, that there is more in gastric analysis than the determination of actual diseased conditions. With these once established, there still remain to be discovered all the individual peculiarities operating in each case. That such should exist lies in the very nature of the complex processes going on along the whole alimentary tract, and is best evidenced in the wide range of the symptomatology, often of a contradictory character, observed in a given number of cases of like pathological basis.

It is in the determination of the average capability of the intact remaining portions of the secretory structures to work that the chief value of gastric analysis lies. Fleiner properly remarks that

it does not make much difference which methods we employ for this purpose, provided they are used systematically, and Trousseau long ago suggested that the correct dietetic treatment of a case of dyspepsia would often depend upon the personal experience of the individual patient.

The necessity for some generally accepted system of examination for the proper recognition and classification of chronic gastric diseases is evident from the variety of opinions which exist as to their relative frequency. For some observers the presence of a small quantity of gastric mucus is sufficient to establish a diagnosis of chronic gastric catarrh. Hence, every third case must be looked upon as such. Others regard chronic gastric ulcer as a common condition, whereas in reality all modern methods of examination have very materially reduced its frequency. Gastric dilatation will be a common disease so long as splashing below the umbilicus is deemed sufficient for its diagnosis, and gastroptosis must be very prevalent if we are to take as signs of its existence a contracted thoracic angle or the floating tenth rib of Stiller. No department of clinical medicine lends itself so readily to fads as gastrology, due partly to lack of uniformity of classification, but chiefly to the absence of recognized system in methods of examination employed and the conditions imposed for the same.

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THE GENERAL MANAGEMENT AND THERAPEUTICS OF NEPHRITIS.[1]

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I shall speak solely of acute and chronic diffuse nephritis. Time does not permit that I refer to the special management and treatment of cirrhosis of the kidney, nor, indeed, to that of lardaceous, or waxy kidney. I shall make few formal citations, and merely an occasional individual reference to others. I shall endeavor to report some of my own convictions in a very brief manner. These convictions are the result of experience and study. Personal papers from which I have again taken observed facts may be found in The American Journal of the Medical Sciences and the *New York Medical Record.*

I am conscious in what follows of imperfect and fragmentary presentation of a very important subject. I trust, however, that numerous gaps and shortcomings will be supplied by others. It must be understood that I could readily amplify many bald statements were more time allotted me, and were I unconscious of the great knowledge of the men who precede.

It is my experience, and I doubt not that of many practitioners, to be called upon only on rare occasions to treat acute nephritis, which is typical according to descriptions in text-books.

The great majority of instances of acute nephritis are grafted on a former process which has existed for some time and which has probably been caused in the first instance by harmful and irregular modes of life, or become developed during the course of some infectious disease. Many of these patients have not been aware that they were suffering from any renal trouble, and it is only when acute symptoms of more or less gravity appear and they seek medical advice that their condition is discovered. At that time and after careful inquiry and research, we shall frequently remain in reasonable doubt as to whether or not the kidneys had been diseased previously, and to what extent the fresh inflammatory process stands by itself. Fortunately, therefore, our methods of dealing with acute, subacute, and in a measure chronic diffuse nephritis are not dissimilar. Wherein differences of management and treatment exist and should be rationally attended to, I shall endeavor briefly to make evident later in this paper.

The first thing to do in all cases of nephritis in which the disease shows acute symptoms is to have the patient go to bed. It is ill-advised to allow him to lie between sheets, particularly linen ones,

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during the first few days of the acute febrile attack. Not only should he be covered on all sides with blankets, but his underclothing should be of wool. A most useful garment is a long woollen night-shirt reaching from the neck almost to the feet. Heat to the surface and of a continuous character and more than is agreeable is imperatively required. No risk even of temporary chilling should be incurred. Of course, this would be much greater in cold than in warm weather. The two cardinal principles to be kept in view are:

1. Physiological rest, so far as possible, to the diseased organ.
2. Relief of function, especially through the supplementary action of skin and bowels.

The first indication is supplied immediately in the best manner by going to bed, as I have stated, because in this way, with perfect repose of mind and body, we do not fear so much the immediate bad effects of mental occupation and muscular effort. Diet, judiciously considered and most appropriate, is the next important direction of meeting the indication. With great initial engorgement of the kidneys it is wisdom to give very small quantities of food, and solely in liquid form. Thus there is much diminished residual waste, and least irritating substances passing through a clogged-up structure. A milk diet, almost exclusively, is the one usually insisted upon during many days or weeks of the primary attack. In my judgment, this dietary should be insisted upon, but with certain limitations proceeding from common sense and experience. There are many people to whom milk is repugnant, with whom it does not agree. This is eminently true of milk in raw, undiluted form; combined with lime-water or Vichy, with the addition of a little salt, peptonized or fermented, as koumyss or matzoon, it may be acceptable to some of this number. With others of the class referred to, one must fall back upon the use of gruels and broths, jellies, and, after a few days, arrowroot, rice, or other light, amylaceous food. Among the diluents, after a day or two, water in abundance may be advantageously taken, and, when given, I am satisfied that good spring-water is especially desirable by reason of its non-irritating diuretic properties. To water may be added without injury, if the patient asks for it, weak tea, lemonade, or water from a slightly alkaline spring. If the œdema or dyspnœa is threatening, or if the urine be suppressed or in small, concentrated quantity, the bowels should be emptied rapidly by a purgative enema, or by repeated doses of salts, compound jalap powder, or calomel. So soon as the bowels have been thoroughly moved, a hot wet pack properly applied, which shall cause abundant perspiration without danger of subsequent chill or undue depression, should be insisted upon. Hot-water baths are very troublesome, are no more efficacious, and are often dangerous when given without extreme care. Hot-air baths given in bed by means of an alcohol

lamp, and hot air conducted under the supported bed-coverings through a metal tube, or according to the newer Zellerman-Sheffield system, have their warm advocates, and, in institutions where the attendants and apparatus may be readily utilized, may prove very desirable. In the care of private patients I greatly prefer the hot wet pack, for its perfect simplicity and saving of fatigue, exposure, and mental anxiety in very nervous patients. Whenever there is local pain over the loins, and especially if the urine is much diminished and of high specific gravity, while containing a considerable amount of albumin and numerous casts, dry cups, or a large, warm poultice of flaxseed, with enough mustard to redden the skin, affords relief and is useful by directing the blood to the surface and decongestioning the kidneys. After the bowels have been freely moved one or more times, high rectal irrigations by means of Kemp's tubes have in my experience promoted diuresis and neutralized toxic substances from the intestinal tract which have been injurious to the inflamed kidneys. I am of the opinion that we have, in the adoption of this later acquisition to our armamentarium, a means, when suitably employed, of very great value. I object to pilocarpine as a dangerous drug to use, as it has occasioned death several times within a few days from acute bronchial or pneumonic symptoms. In one notable case, after childbirth, in my own experience, its use induced, in a very short time, excessive secretion in the bronchial tubes, and death promptly occurred.

If threatenings of uræmia are shown by increased tension in the arteries, an accentuated aortic second sound and perhaps preliminary muscular twitchings, a few doses of nitroglycerin will often relieve the situation very rapidly. Whenever such is the case, I am inclined also to order repeated doses of sweet spirit of nitre, or to add a teaspoonful to a tumbler of water, and request the patient to drink a mouthful of it every hour or two. The nitre relaxes the arteries, acts as a diaphoretic, and is effective and innocent. In its action upon small vessels it may be regarded essentially as nitroglycerin and the nitrites. If there is a real uræmic seizure, either in the form of a clonic convulsion or of a rapidly developing comatose state, abstraction of blood, either by bleeding from the arm or wet cups over the loins, will sometimes be the only means of saving life. After several ounces of blood—*i. e.*, from 8 to 20—have been taken, it is often desirable to infuse through the veins with hot saline solution. By doing so we rid the blood, on the one hand, of a certain amount of virulent toxic material that is overwhelming it, and on the other we dilute this toxin in the most approved manner so as to allow the nervous system to support it until we can clear the organism by other efficient, though slower means. In a few instances it may be necessary to recur to inhalations of chloroform, injections of chloral hydrate by the rectum, or the hypodermic use of morphine. I have less formal objections to the use of morphine subcutaneously

in the uræmia of acute nephritis than I have in the chronic forms; still, I am ever loth to recur to it unless absolutely indicated by the extremity of the case. In certain eclamptic seizures I might advise it, especially when the seizures are frequent and I believe I have to do with puerperal nephritis, and not with acute nephritis.[1]

And yet even in these instances, and although morphine injections appear to diminish the frequency of the convulsions, when given before delivery they undoubtedly add to the risk of the child. In some of these cases I am convinced that repeated inhalations of oxygen are very valuable in avoiding the manifestations of uræmia, and in promoting its cure when fully developed. In more than one example it seemed as though just the food for the poisoned red corpuscles was being supplied. As the acute stage passes, the fever disappears, albumin and casts are diminished, and blood cells are no longer found in urine, we may become less rigid about absolute rest and diet. An egg, fresh fruit, bread, a little fish, some light puddings and green vegetables may be added to the milk dietary. Also, the patient may be permitted to sit up, or move about a little each day. For the anæmia, which is often very pronounced, some good preparation of iron is desirable in moderate doses. Of these none equals the tincture of the perchloride, either with a little glycerin, spirit of chloroform and water (Reynolds' mixture), or under the form of the well-known Basham mixture, in which it is combined with spirits of mindererus. In the same way as we require iron, oxygen, more and appropriate food, as the disease becomes subacute or chronic, so we must have good fresh air and plenty of it for these patients. Those whose means permit should seek, when otherwise possible, a warm, dry, equable climate, where their life should be passed mostly in the open air, and away from fatigue, mental and bodily. Whenever it is impossible to remove these patients from their surroundings, it is incumbent upon them to avoid cold, damp weather, and when they are unfortunately exposed to it, to be warmly clad so as to resist the effects of atmospheric changes, particularly of any draughts of air to which they are peculiarly susceptible. The albuminuria itself may persist for a long while, and, indeed, may be most difficult to overcome. We have no remedy which has any direct effect probably in promoting curative changes of diseased kidney structure, and we should expect decided amelioration, if not cure, mainly through ambient surroundings of healthful and suitable character, great and continued attention to proper dietary, the use of plenty of spring-water, suitable woollen underclothing, proper, well-prepared food, and promotion of good nutrition by the use of hæmatinics and avoidance of undue fatigue and worries. From time to time it is desirable to keep the skin active by means of the wet pack or hot-air bath, and under

[1] If the quantity of blood in the urine, in addition to the amount of albumin, is considerable, the latter diagnosis is probably correct.

no circumstances should the bowels be permitted to become at all constipated. Every effort should be made to avoid chilling of the surface, undue physical effort, absorbing mental preoccupations, imprudences of diet and régime. Secondary thoracic inflammations of acute nephritis are often very threatening and difficult to treat. They occur at a time when the patient is already depleted and would bear antiphlogistic remedies badly. Moreover, they run their course rapidly and with great severity. Moderate counter-irritation to the chest walls or more distant parts is useful, but we must beware of causing blisters. We should also be careful about remedies like turpentine, which even locally may occasion renal irritation. If despite everything the acute nephritis has remained uncured and become a condition of chronic diffuse nephritis, there are some special indications which I would further emphasize. First, in regard to the condition of the stomach and intestines. Second, in regard to the skin when it becomes tense and unduly distended despite all the means hitherto employed to promote absorption. Nausea and repeated vomiting may become, both in chronic and acute nephritis, a factor of the disease which requires our most careful treatment. After other means have been exhausted, I have occasionally found that repeated small doses of Kirschwasser have been signally successful. This water, so-called, is nothing more (as you know) than a dry alcohol containing prussic acid from peach-kernels. Chlorodyne, in repeated minute doses, diluted with a little water, has helped me at times in a remarkable manner. The diarrhœa of chronic Bright's disease is combated, as I believe, when other means fail, with occasionally surprising good effects by means of prolonged intestinal irrigation with hot saline solution.

When œdema to an excessive degree exists and affects the lower limbs, in order to prevent the breaking of the skin and resultant ulceration, it is desirable to use the lancet and make several punctures, or incisions, under antiseptic precautions. Subsequently, the limbs should be frequently washed with some mild disinfectant solution and bandaged. Occasionally it is desirable to insert a small capillary tube under the skin and leave it *in situ* for a while, after connecting it with a rubber tube of small calibre, so as to carry on continuous drainage into a vessel near the bed. Of course, such punctures, or the insertion of capillary tubes, may occasionally be followed by erysipelas or local gangrene, despite every care and precaution. Withdrawal of fluid from the pleural cavities by aspiration, when the heart is pressed upon and there is marked dyspnœa or paracentesis of the abdomen, when there is great distention of its walls, or the slow withdrawal of fluid from the peritoneal cavity by means of a small cannula, left in place several days, are at times clearly indicated and required. The use of the alkaline diuretics, such as the citrate and acetate of potash, or the

use of a subacid drink with cream of tartar and lemon-juice, is frequently very beneficial when the acute stage has subsided, and there are no longer any blood cells in the urine. The former salts eliminate themselves from the economy under the form of carbonates, and when continued for a while, unless they upset the digestion notably, may ward off the development of uræmic symptoms. Such is the judgment, at all events, of many careful observers. Whenever the heart has become dilated and weak, the quantity of urine is notably increased, the circulation strengthened, and the patient's general condition improved by means of digitalis, strophanthus and, strychnine in suitable doses. In febrile conditions, and especially among the gouty and men past the meridian of life, digitalis can rarely be given with advantage, without being protected as to its action on the peripheral arterial circulation by corrective doses of nitroglycerin. Otherwise we are apt to get a bounding, tense pulse which frequently forebodes ill for the patient, unless it be neutralized rapidly by the proper medicinal agent. A point of considerable importance, often overlooked, is to avoid, in the treatment of the pyrexia, the use of certain drugs, like chlorate of potash or salicylate of soda, whenever there is distinct evidence of nephritis, because of their well-known irritative action upon the kidneys. In the matter of diet it is wisdom in every case to watch closely the amount of albumin and number and nature of casts passed in the urine from day to day. The personal factor enters here as in the rational treatment of all disease. Thus, while in the experience of some, when the nephritis becomes subacute or chronic, albumin is stated to be notably increased by allowing one or more eggs daily to the patient, it is the experience of other competent observers that with this addition to the diet the albumin eliminated in the urine will diminish in quantity very soon, and the patient will gain in color and strength and appear to be generally improved in health. In the administration of any one of the iron salts we should ever be alive to their constipating effects, and likewise to the injurious results proceeding from overdoses, as insisted upon by Tyson. Attention should be directed to the fact that in the infectious diseases, such as eruptive fevers, diphtheria, typhoid fever, pneumonia, etc., the determination of the disease upon the kidneys marches *pari passu* with the action of its toxins upon other organs. Therefore, we should not be prone to interpret the evidences of nephritis (albumin, casts, etc.) as of too threatening nature in many instances, nor change our general method of treatment much or at all, on account of the renal symptoms. When the fever abates, or convalescence is established, the renal signs and symptoms clear up as a rule, and become satisfactory in the same way and according to the same lines that other morbid manifestations of the special infection do. Of course, there are instances in which the symptoms are specially threatening from the renal standpoint, and not infrequently

I have noticed symptoms which I have felt convinced were clearly uræmic in nature. While such cases, if unobserved, or ignorantly treated, might go from bad to worse and result fatally very soon, when the symptoms are intelligently treated they usually improve by degrees, always presuming that the kidneys were normal prior to the *début* of the infection. In this connection I would direct attention to the grave form of typhoid fever beginning with nephritis and intense gastrointestinal symptoms. Here we should not be misled as to the seriousness of the infection from every point of view, the renal condition being included, of course, with the rest. In all cases of prolonged albuminuria following acute nephritis great care against cold, exposure, and imprudences of diet, as well as against overwork and fatigue, must be exercised so as to prevent, if possible, the development of chronic nephritis. If, despite all precautionary or prophylactic measures, chronic nephritis develops, we should be especially solicitous about all subacute complications; and whenever the urine shows, by increase of albumin or casts, and especially by the presence of blood casts or free blood cells, this condition, the patient should be put to bed and treated essentially as already indicated. Chronic nephritis is frequently an incurable disease, and in any event we should not expect too much from the purely medicinal measures. Some cases do eventually recover, but when this is the case, the cure should be attributed rather to the continued close observance of hygienic rules than to the influence of remedies. The best that we should usually hope for is the improvement of the kidneys functionally as well as of the work of the organs secondarily affected. Of course, as far as may be, it is desirable to treat the cause of the chronic nephritis, but frequently this is difficult or impossible, and the disease is already well established when we first recognize it. However, whenever syphilis, malaria, or suppurative processes are present, we should not ignore the indications which proceed therefrom. We must, however, always bear in mind that many of the drugs employed to relieve those conditions are inimical to the healthful action of the kidney, and may indeed increase albuminuria and hæmaturia. Notably this is true of many of the so-called disinfectant remedies, such as carbolic acid, salicylic acid, and the salicylates, sulphocarbolate of sodium, etc. Therefore, even when we are warring against the autointoxications of gastrointestinal origin, we should bear these facts in mind, and likewise the fact that with any reasonable or non-poisonous dose of these drugs it is extremely doubtful whether we can entirely destroy infective micro-organisms which go to the kidneys from the stomach and bowels, or originate, indeed, within these organs.

While it is relatively easy to point out the dangers and drawbacks of unwise medication, it is difficult to say what medicinal remedies are useful in ameliorating or curing the disease. Chronic nephritis

comes on so gradually, so insidiously, and withal is typical of such a low grade of inflammatory action, that we know of no drugs to which we may recur with hopeful trust as to their real efficacy. It is doubtful in many instances of chronic nephritis whether it is wisdom to keep the patient closely confined either to his bed, his room, or the house. Too close confinement, even though theoretically the renal functions are thus relieved, will finish by diminishing appetite and undermining strength. Therefore, when the nutrition is fairly maintained, the strength sufficient, and the dropsy only moderate, it is better to advise gentle exercise in the open air whenever the weather is favorable. Under other circumstances, and especially whenever an acute complication has arisen in any organ, close confinement to bed, or one's room, should be insisted upon during its duration.

Fürbringer has shown the wisdom of the former counsel, and where the skin was acting freely, in one notable case. Whenever the disease itself presents atypical features, or any particular symptom is prominent or threatening, special indications of treatment may arise. It is well to remember in all such cases, that while in appearance we may be dealing with or caring for only a single manifestation of chronic nephritis, we may in reality be dealing rationally and successfully with the disease considered in its entirety. Thus, for example, in treating excessive albuminuria or dropsy, diminution in quantity of urine, sudden amaurosis or uncontrollable vomiting, we may be doing our best work for all the symptoms and conditions involved in the special case of chronic nephritis. Among remedies which have been vaunted to increase the quantity of urine in chronic nephritis, without, however, notably diminishing the amount of albumin, is iodide of potash. Ringer insists upon its efficacy in this direction independently of a syphilitic causative factor in the case. Further, he insists that in many instances the amount of iodide taken daily so as to secure its best effects must be increased to 100 or even 200 grains. I have never given such large doses, nor should I be inclined to do so except in very rare instances. The majority of patients affected with chronic nephritis have a very sensitive stomach and bowels, and the iodide, even in moderate doses, is apt to derange them. Further, its unpleasant after-taste, particularly, no matter in what manner we administer it, is apt to cause considerable annoyance and diminish appetite to a marked extent. The question of the amount of albumin eliminated daily is closely related to that of the proper diet for the patient. Some physicians hold that the dietary should be of the sort which shall not tend to increase the amount of albumin lost, as they believe the loss of strength of the patient is mainly due to this fact. Others with, as I believe, equally good reasons hold that it is far wiser to compensate for this excessive drain of albumin from the blood by increasing the quantity and variety of the food,

and thus maintaining the patient's strength and vigor. It seems to me that much must depend as to our guidance upon the individual case. If headache, malaise, interference with normal digestive processes are evidently occasioned by increased dietary, it should be abridged considerably. If, on the contrary, there are no unpleasant and untoward sequelæ other than the large daily excretion of albumin in the urine, and if, moreover, the patient's general health and strength seem satisfactory in view of the nature of the case, it seems the part of good judgment to persist in a more liberal dietary. Of course, if in the course of chronic nephritis acute hyperæmia should occur, and blood again appear in the urine, it is obviously and formally indicated to return to a liquid diet, mainly of milk, until all acute symptoms have again disappeared. It is objected to the increase of diet in chronic nephritis, that there are some instances on record in which long persistence in a milk diet had apparently cured the disease. George Johnson, for example, has cited a case in which this result followed after a period of six years.

In general, nephritic patients are better off without alcohol in any form—still there are exceptions. In men and women of middle life who have been accustomed to take a glass of wine or a little whiskey and water at meals for many a long year, it is unwise, as I believe, to intermit the habit. By so doing their appetite and digestion would be impaired, they would take less food, and, moreover, become introspective, morbid, or depressed.

In regard to the choice between spirits or a good, sound wine or light beer, I believe it may be left often to individual fancy or desire. The essential matters are that stimulants should be taken, as a rule, only at meals, in small quantity, and diluted. Of course, if there has never been the habit of taking alcohol in any form with the meals, it is unnecessary and may be harmful to begin it. In instances in which there is decidedly lowered heart power, general weak circulation, and notable exhaustion, small quantities of alcohol, both as food and stimulant, should be given for a time and the effect upon the renal condition may be considered secondary to other major and imminent considerations. Occasionally, no doubt, the amount of albumin diminishes during the period the patient is taking some astringent drug. It always seems to be a *post hoc, ergo propter hoc* proposition, and I am usually of the opinion that the dietetic and other general rules laid down and observed have been more useful than the remedy employed. It is certain, in any case, that when the astringent causes inappetence or stomachal distress it should be intermitted. Even in those cases in which an acute process has intervened and there is quite abundant hæmaturia, I am confident light diet, warmth in bed, and absolute physiological rest as far as may be to the diseased kidneys have played a far more important and beneficial role than the astringent drug. Just

as in interstitial nephritis our greater fears come frequently from dangerous uræmic manifestations, so in chronic diffuse nephritis at a later stage the presence of large dropsical effusions is often a source of much anxiety. In the lower limbs or in the peritoneal cavity they occasion much discomfort, but they do not threaten life by direct interference with heart action, as large effusions of the pleuræ sometimes do. I have already alluded to the different medical ways of relieving this condition, their indications and objections. To repeat: they are hot-air baths or wet packs, possibly the use of pilocarpine in minute doses hypodermically, hydragogue cathartics and alkaline diuretics. Whenever all these fail and the condition of the patient is imminently threatening we make use of surgical procedures—*i. e.*, puncture of lower limbs, paracentesis of abdomen, or aspiration of pleura, according to what seems first of all required. In the most severe dropsical conditions I have many times tried all these seriatim. Uræmia, especially the chronic form, not infrequently occurs in chronic nephritis in the later stages when the kidney is contracted. It should be treated very much as we do the dropsical symptoms, barring the surgical procedures just mentioned. In acute uræmia when convulsions appear, purgatives and the hot pack may be employed. Chloroform inhalations may also be used immediately to shorten the attack. I am not convinced, however, despite much testimony to the contrary, that they will accomplish this result. The use of morphine in the treatment of uræmic convulsions is still a moot question before the profession. The late Dr. A. L. Loomis cordially supported its use. Professor Wm. Osler is to-day a warm advocate of its employment, and holds that he has never seen it do harm. Delafield, Musser, and Tyson endorse its use in certain cases, but restrict its indications somewhat. Tyson believes it to be particularly harmful in interstitial nephritis.

On the other hand, George Johnson and Tirard are unqualifiedly opposed to its use in chronic nephritis in either form, and claim that as a result of hypodermic injections of morphine the convulsions become more frequent and more severe. For my part, I am of this opinion in those instances in which the convulsive seizure is accompanied with the *contracted pupil.* Whenever the pupil is *dilated,* or even of *normal size,* I have seen small or moderate morphine injections of evident service. In the other instances I have seen it act in a similar way to that pointed out by Johnson.

In this connection I would add that I am much pleased to note that Holt, in the last edition of his admirable book on *Diseases of Children,* emphasizes the indication which proceeds from the size of the pupil in the use of morphine in uræmia. Morphine injections may indeed be given and promptly followed by the arrest of a convulsive seizure. Yet too often this arrest is but the prelude of a rapidly fatal ending. Perhaps this sad result might be averted, as suggested by B. K. Rachford, if immediately after the use of

morphine blood be withdrawn from a vein and followed by intravenous saline infusion.[1]

As a rule, where there is much sleeplessness, I prefer the bromides to chloral, as in cardiac weakness the latter drug is invariably dangerous. Whenever the condition is imminent and there is high-tension pulse and a fairly vigorous patient, venesection, followed by intravenous infusion with hot, sterile, saline solution, will relieve acute uræmia at times as nothing else will. I have seen almost miraculous cures from this procedure which I have had occasion to have done for me many times. There are numerous occasions when I prefer high rectal enemata to intravenous infusions. My experience with subcutaneous injections of saline solutions is not at all favorable. They are far more painful than is stated, and their immediate or remote effects upon the uræmic poison have not appeared to me as desirable as those derived from infusions or enemata.

One very important precaution in the use of saline infusions is to guard against dilatation of the right heart, a complication to which Tyson and I have directed attention. The indications proceeding from the heart and pulse in chronic uræmia call often for a heart stimulant, and digitalis and strophanthus are frequently used.

During many years and in some of my worst cases of weak heart relaxed arteries, dropsical effusions, and insufficient urination, I have found Trousseau's diuretic wine invaluable. As is well known, it is composed of digitalis, squills, juniper berries, acetate of potash, and white wine.

We are sometimes compelled to stop all medication by the mouth in view of uncontrollable vomiting. Life is then supported almost solely, at times, with nutrient and other enemata. What I have written applies in general terms to the management and treatment of chronic nephritis in childhood as well as in adult life, except that hot tub-baths may be given more easily and safely to children than to men and women. With children the undue use of hydragogue cathartics on account of their weakening effects should be specially avoided. On the other hand, they bear repeated doses of mercury in nephritis perhaps better than adults, and run less risk of salivation. This accident, as we know, should be dreaded with the latter, on account of their extreme susceptibility to the physiological effects of the drug (Roberts).

In view of late investigations by Widal and Javal, it would seem as if it were most desirable to suppress entirely the use of salt in the dietary of patients affected with acute or chronic nephritis whenever the dropsy is considerable. These experimenters have also shown the great value of theobromin as a diuretic to diminish albuminuria, and to benefit the general condition of the patients. The inferiority

[1] Medical News, March 15, 1902.

of digitalis, nitre, and squills in these regards is insisted upon. "A mixed diet, the authors agree, without salt, may safely be given to nephritics."[1]

Finally, Dr. McVail, of Glasgow, reports two cases, one of convulsions, the other of coma, in which successful results followed spinal puncture when other means failed. In his opinion these instances prove that convulsions and coma in acute nephritis are due frequently "to the sudden increase of intracranial pressure, and not to uræmic poisoning of nerve centres."[2]

PALSY OF THE EXTRAOCULAR MUSCLES IN EXOPHTHALMIC GOITRE.[3]

WITH THE REPORT OF A CASE.

By William Campbell Posey, M.D.,
of Philadelphia.

In addition to the usual ocular signs which constitute part of the cardinal symptoms of Graves' disease—*i. e.*, the exophthalmus and the so-called Graefe, Stellwag, Dalrymple, and Möbius signs, and which are dependent upon various inco-ordinations and weaknesses of certain parts of the nervous mechanism of the eye, actual palsy of one or more of the extrinsic ocular muscles is sometimes met with. The notes of a case of this nature are appended.

Sarah L., a housekeeper, aged forty-three years, was brought to the service of the writer at the Polyclinic Hospital by Dr. O. C. Heffner, of Pottstown, Pa., in October, 1902, upon account of poor sight of several months' duration. The patient had been in rather poor health for ten years or more, suffering from palpitation of the heart and nervousness, but had had no prolonged or serious illness other than attacks of muscular rheumatism. Her appetite was good and her bowels regular; she still menstruated regularly, though she had always been subject to more or less uterine trouble. She had had seven children, five of whom were living and well; she had had no miscarriages. She said that her sight had always been good until two months before, when she suddenly saw double, the double vision persisting without remission ever since. Though dizzy at times, she did not complain of nausea, nor was she subject to attacks of vomiting. She had suffered considerably from supraorbital and temporal head pains for several years, which were at times quite violent.

[1] New York Medical Journal, November 7, 1903; and La presse médicale, October 7, 1903.

[2] British Medical Journal, October 24, 1903, p. 1054.

[3] Read before the Ophthalmological Section of the College of Physicians of Philadelphia, January 19, 1904.

She was not aware of ever having had a swelling of the neck. Dr. Heffner had noticed a prominence of the eyes, especially of the left, for several months previously. Upon examination both eyeballs were found to be slightly proptosed, the left being slightly more so than its fellow. As shown in the accompanying photograph, the palpebral fissures were widened, there being about 2 mm. of white sclera showing between the upper lid and the superior border of the cornea in both eyes. It was noted that the patient fixed with the right eye, the left being rotated somewhat downward and out-

Exophthalmic goitre, showing exophthalmus, the Dalrymple sign, and paralysis of the external, superior, and inferior rectus and inferior oblique muscles of the left eye.

ward. The Graefe lid sign was at times present in both eyes, but at others, though carefully searched for, it could not be demonstrated. When the patient was asked to follow the examiner's finger in testing the excursions of the eyes, it was found that the left eye could not be rotated above the median line; external and internal motion also was restricted; downward movements were good. All of the motions in the right eye were performed normally. The pupils were 3 mm. in size and the irides responded equally and freely to light and accommodation stimuli. The ophthalmoscope showed about 1 D. of hypermetropia in each eye with some astigmatism. The optic nerves were somewhat gray, but there was no

neuritis. The retinal veins were rather fuller than normal and pulsated upon the disk only. Vision equalled 5/6 in the right eye and 5/9 in the left. There was no restriction of the visual fields.

From a study of the double images, it was apparent that there was a palsy of the left sixth nerve and of that portion of the third nerve of the same side which supplies the inferior oblique and the superior and inferior recti muscles. The patient was referred to the nervous clinic of the hospital for further study, where Dr. Spiller examined her, with the following result: "Patellar reflex exaggerated upon each side. Ankle clonus not obtained on either side. Achilles reflex in Babinski position distinctly exaggerated on each side and equal. Babinski reflex doubtful on each side, toes not moving distinctly in either direction on irritating sole of foot, tendency being to extension. Resistance to passive motion in lower limb not diminished in leg or thigh on either side. Sensation for touch and pain normal in all parts of body. Grasp of hand normal on each side. Triceps tendon reflex, biceps tendon reflex, and wrist reflex exaggerated and equal on each side. Gait normal. Station erect, normal, even with eyes closed. Motion of upper limbs normal in all directions. Resistance to passive movements at elbows normal. Tongue protruded straight in median line and movements free in all directions; no marked atrophy; no fibrillary tremors. Movements of facial muscles normal on each side. Patient has difficulty in drawing either corner of mouth upward separately, but in showing teeth the muscles of mouth are drawn up well. The eyelids are closed normally and the forehead wrinkled properly on each side. Masseter contracts firmly on each side. Sense of smell seems to be intact. Hearing seems to be good on both sides. Pulse 110 to 120. Slight prominence of thyroid."

An examination of the urine showed specific gravity 1026; no albumin or sugar.

A diagnosis of Graves' disease with the unusual finding of palsy of the extraocular muscles was made, and with the concurrence of Dr. Spiller the patient was advised prolonged rest in bed and specific treatment. This was adopted, but after a few weeks' trial the patient tired and left the hospital without any apparent change in her condition.

Instances of palsy of the extraocular muscles in Graves' disease are rare, but a search through the literature reveals a number of cases somewhat similar to the one just reported. Quite lengthy reference to these may be found in several interesting monographs, of which the most notable are by Ballet,[1] Liebrecht,[2] Buschan,[3] Mannheim,[4] and Möbius.[5] It would appear, from the cases reported and cited by these authors, that the paralysis may affect a single

[1] Gaz. hebd., 1888, p. 558.
[2] Klin. Monatsbl. f. Augenheilkunde, 1890, p. 492.
[3] Dissertation, Leipzig u. Vienna, 1894.
[4] Dissertation, Berlin, 1894.
[5] Zeitschr. f. Nervenheilkunde, vol. i. p. 460.

muscle or group of muscles of one eye, or even all the extrinsic muscles of one eye; and that occasionally one or more muscles of both eyes are simultaneously affected. Palsy of the ciliary muscle or iris is not recorded; nor of any of the associated movements of the eyes with the exception of reports by Schmidt-Rimpler[1] and Vossius[2] of cases of paralysis of convergence. Palsy of the levator palpebræ superioris in conjunction with palsy of the other branches of the third nerve is rare; but is rather more common without such association. The palsy may come on early in the course of the disease, but in most cases it is a late manifestation; though usually persistent, it may be but a transient condition, the muscles regaining their full strength.

The palsy may occur without paralysis of other cranial nerves, or it may be associated with a similar affection of one or more of them; thus Bristowe[3] has recorded the case of a young man who developed the symptoms of ophthalmoplegia externa three years after the ordinary symptoms of Graves' disease had manifested themselves. There was also right hemianæsthesia, with color blindness and loss of taste and smell on the same side, some palpitation and dyspnœa with headache and sickness. After a period of some months, epileptic fits came on, and later on hemorrhages from both ears. Death finally occurred from bronchitis. Autopsy was negative.

Similarly in a case reported by Warner[4] there was binocular external ophthalmoplegia with palsy of the facial and trigeminal nerves. Jendrassik[5] saw paresis of the muscles of mastication in addition to palsy of the rotary muscles of both globes, as well as most of the muscles of the face and palate. Of interest in this connection also are four cases reported by Ballet:[6] the first, the subject of severe hysteria, in addition to ophthalmoplegia externa, presented a number of bulbar symptoms—*i. e.*, palsy of both facials and paresis of the hypoglossus. In the second, also the subject of severe hysteria, there was right-sided hemianæsthesia and loss of smell and taste on the same side. Autopsy showed no visible change in the central nervous system. In a third case, in addition to palsy of both external rectus muscles, there was right-sided hemiplegia and hemianæsthesia, with epileptic attacks. The fourth case was an instance of ophthalmoplegia externa with paresis of the facial and hypoglossus. Chevalier[7] saw palsy of the externi and oblique muscles associated with disturbance in the supply of the fifth and seventh nerves and of speech.

In a case of Maude's[8] the lesion seemed to spread over the entire

[1] Nothnagel's System, 1398.
[2] Beiträge zur Augenheilkunde, 1895, vol. xviii.
[3] Brain, 1886, p. 313.
[4] Medical Times and Gazette, 1882, p. 540.
[5] Arch. f. Psych., 1886, vol. xvii. p. 301.
[6] Loc. cit.
[7] Thesis, Montpellier, 1891.
[8] St. Bartholomew's Hospital Reports, 1892, vol. xxvii.; also Brain, 1892, Autumn, p. 424.

region of the nuclei of the extraocular muscles, and those neighboring upon them, paresis of the external rectus, and probably of the superior oblique, being preceded by palsy of the facial and quickly followed by general ophthalmoplegia.

Stellwag's[1] case was one of paralysis of the lateral rotators (the ocular axes being parallel and convergence undisturbed) and later palsy of both externi with convergent strabismus and diplopia developed with transient anæsthesia and restricted movement of the left half of the upper legs.

In a case reported by Féréol,[2] of a man, aged forty-one years, six months after the appearance of the initial symptoms of exophthalmic goitre, there were headache, vomiting and dizziness, tremor, with disturbed gait and a disposition to face to the right; then diplopia, the result of right-sided trochlearis palsy. There was also right-sided diminution of motion and hyperalgesia, while on the left side there was a diminution in sensation of pain.

In a recent number of the *Deutsche medicinische Wochenschrift*, August 13, 1903, Voss, of St. Petersburg, has reported two additional cases of palsy of the extraocular muscles in exophthalmic goitre. The palsy in the first case had affected the superior and external rectus muscles of the right eye and the inferior and external rectus muscles of the left eye. There was also a partial palsy of the right facial nerve, with some cerebral symptoms.

The second case exhibited multiple lesions in the muscles of both eyes, the superior rectus muscle of the right eye being particularly affected.

The same author refers to a case of Bartholow where there was ptosis in association with gangrene and neuritis of the lower extremities.

Dyson[3] reported a case of a man with the symptoms of incipient Graves' disease, in which, in addition to slight exophthalmus and Graefe lid signs, there was slight internal convergent strabismus and dilatation of the pupil of the left eye. The patient was a chronic alcoholic.

Bruns[4] saw ptosis on the left side, with palsy of the superior recti in both eyes, with the cardinal symptoms of exophthalmic goitre, but as the patient was the subject of a chronic nephritis, it was thought that the nuclear lesion might be referable to this source and not to the Graves disease.

Wilbrand and Saenger[5] report a case with slight ptosis on the left side; with retraction of upper lid, with Graefe lid sign, upon the right side. This was explained by a bilateral affection of the nuclei

[1] Wien. med. Jahrb., 1869, p. 25.
[2] Gaz. hebd., 1889, p. 112.
[3] British Medical Journal, January 15, 1887.
[4] Anzeigen zur Zeitschrift für Psychiatrie, Bd. lx., Heft 5.
[5] Die Neurologie des Auges, vol. i. p. 47.

of the levator—*i. e.*, an irritation of the levator on the right and a palsy on the left side.

De Giovanni[1] has reported a case of unilateral exophthalmus, as a consequence of palsy of the extraocular muscles, especially of the rectus superior, in which goitre and other classical symptoms of Graves' disease were present.

In addition to these cases of more or less complete ophthalmoplegia externa, others, though more uncommon, of palsy of a single eye muscle have been reported. These have been grouped by Buschan[2] as follows:

1. Cases in which diplopia was complained of, but the muscles at fault not ascertained: Trousseau Smith, Chvostek, Stellwag, Impaccianti, Strümpell, F. Müller, and Lang-Pringle.

2. Cases of palsy of the rectus internus: West, Homén, Cohen, Westedt and Romberg, rectus interni of both eyes; Schoch and Rothmann, rectus internus and externus.

3. Cases of palsy of the rectus externus: Kurella, Mackenzie (several cases), Eulenburg, Stellwag, Makeig Jones, Liebrecht, Dyson, Ballet, and Cohen.

4. Cases of palsy of the rectus superior: Sollier, Fischer-Degranges, Kahler, Roth, Schlesinger, and Chvostek.

5. Cases of palsy of the trochlearis: Féréol.

6. Cases of palsy of the levator palpebræ of both eyes: Maude and West.

It is evident from a recital of these cases that palsy of the extraocular muscles is not of very rare occurrence and as such is not to be considered as accidental but rather as part of the morbid process of Graves' disease. Just what this part is and what the character and where the seat of the lesion may be, cannot in the still uncertain state of our knowledge regarding the nature of Graves' disease be asserted with certainty, though it would appear at least that in those cases where there was more or less complete ophthalmoplegia externa, and especially in those in which there were associated lesions in the facial, hypoglossus and glossopharyngeal nerves, that the palsy was of central origin, originating in the nerve nuclei. This reference of the palsies to an involvement of the nerve nuclei is an observation of great interest bearing upon the pathology of Graves' disease, for it is additional proof of the central origin of the affection; and while the nature of the morbid process in the nuclei which occasions the extraocular palsies is still to be determined it is probable, as the palsies are sometimes transient and the autopsies which have been made (Bristow, Ballet) have failed to reveal any visible pathological change, that the morbid process is only functional, consisting of an irritation of the centres

[1] Referat aus der Deutschen medicinal Zeitung, 1889, No. 98, p. 1143.
[2] Dissertation, Leipzig and Vienna, 1894.

by toxins which may, as evidenced by the pathological changes which occur in the thyroid gland in so many of these cases, be generated in the system as the result of some perversion in the normal action of that structure.

SKETCH OF THE EXTERNAL APPEARANCES OF UVEITIS FROM CONGENITAL SYPHILIS.[1]

By Charles A. Oliver, A.M., M.D.,
of Philadelphia.

The accompanying sketch, made by Miss Paula Himmelsbach, of this city, is so faithful a representation of the ocular changes visible externally in uveitis from congenital syphilis that it is herewith reproduced.

I first saw the patient some fourteen years ago, when she came to the clinic of Dr. William F. Norris, at Wills Eye Hospital. At that time she was a small, somewhat deformed girl of ten years of age, who, presenting all the stigmata of inherited syphilis, came to be treated for a gross attack of interstitial inflammation of the left cornea, the right one having been attacked and apparently cured in three or four months' time some three years previously.

I did not again see her until two years ago, when she reported to my own clinic at the hospital to obtain a re-correction for lenses which she had obtained in the eye dispensary of the Jefferson Medical College some six years previously, and which had been uncomfortable for about three or four months' time.

In the woman I recognized the child of fourteen years before: the same scaphoid curve of the face; the sunken nasal bridge; the cicatrices at the angles of the badly-shaped mouth; the misshapen jaw; the large protruding eyeballs, and the protuberant forehead —all made an indelible physiognomical picture. Small, active, quick and energetic, she seemed not to have developed or grown from what I had once known her; this in spite of marriage and delivery by Cæsarean section some several months previously of a living full-term and apparently healthy child.

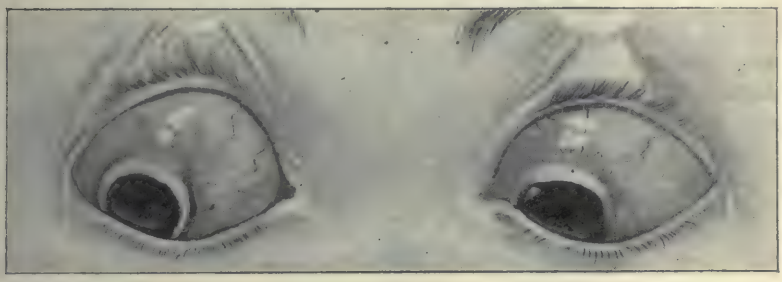
Her teeth, which were small and badly developed, gave none of the gross classical signs of configuration, though the family history, which I had obtained when I first saw her, was undoubtedly that of parental syphilis with its evil effects upon this and two other later children.

Corrected vision and accommodation were normal. Color percep-

[1] Exhibited at the March, 1904, meeting of the Section on Ophthalmology of the College of Physicians of Philadelphia.

tion was good, though possibly there were some slight uncertainty in the finer differentiations of greens and reds. The visual fields were somewhat contracted concentrically. The pupils were irregular (two by three millimetres in size); the irides, which were markedly depressed, were prompt in their various reactions. The anterior chambers were deepest in the positions corresponding with their angles and the pupillary areas. There were not any synechia nor marks of previous ones. The iris stroma was thinned, and the crypts were stretched and elongated in many places. The movements of the eyelids were normal. The action of the exterior ocular muscles was good in all of the ordinary physiological directions.

The corneæ presented some fine canalization which could be discerned only by most careful focusing. The corneal borders



External appearances of uveitis from congenital syphilis.

were densely hazed, particularly above, the dense ring-like opacity passing into comparatively clear though excessively thinned and protuberant peripheral borders. The intraocular media were transparent. The retinæ and underlying chorioids were in comparatively good condition, with the exception of a few fine inflammatory sequelæ and degeneration scars, which were situated well anteriorly and to the lower inner quadrants of the membranes. In places the ciliary regions were thinned and opalescent, but there were not any distinct ectasiæ. The anterior scleral veins, and, in places, the corresponding overlying subconjunctival and conjunctival ones, were engorged and tortuous. The eyeballs were rather large, though apparently symmetrical in their relative diameters.

ACTINOMYCOSIS OF THE TONSILS,

WITH SOME REMARKS ON THE PORTALS OF INFECTION.

By Jonathan Wright, M.D.,
of New York City.

(From the Throat Department of the Pathological Laboratory of the Manhattan Eye and Ear Hospital.)

The only report I can find in literature of the lesion in this situation is by Ruge, in 1896,[1] a member of Gerhardt's clinic. He described four cases, which, wonderful to say, he discovered by the microscopic examination of only twenty-five tonsils. He suggested that systematic examinations of excised tonsils would more frequently reveal the condition. On a reference to my index I find that I have examined microscopically hypertrophied faucial tonsils from more than seventy-five cases. This is the only one in which an actinomycotic clump was present in the sections. It is possible of course that if the whole of every tonsil was reduced to sections, something of Ruge's prediction might have been observed. The clumps, or, as the Germans call them, the "drusen," are not to be mistaken by anyone accustomed to histological work. In a search through the *Centralblatt für Laryngologie* since its first number, a matter of twenty years, only one other reference was found to the existence of a local lesion of actinomycosis in the tonsil, though abscesses and infiltrations around the jaws and neck are cited in great abundance. With the report of this case I am familiar only in references,[2] it having been published originally by Lesin in the Russian *Wratsch*. This latter case died of cerebral involvement and a focal abscess was found in one tonsil and a scar in the other. Ruge concluded, from the fact that his cases presented no lesion elsewhere and had no subsequent trouble after excision of the tonsils, they could only be something that resembled actinomycosis, and reported them under the title "Ueber Actinomyces-ähnliche Gebilde," etc.

Therefore, if rarity of occurrence is any excuse for the publication of this case, I might be justified on that ground alone, but a "rare case" which fits into no category and teaches no lesson furnishes idle reading and is a futile labor for the author. The fewer such facts a man has to put in his mental storehouse the better.

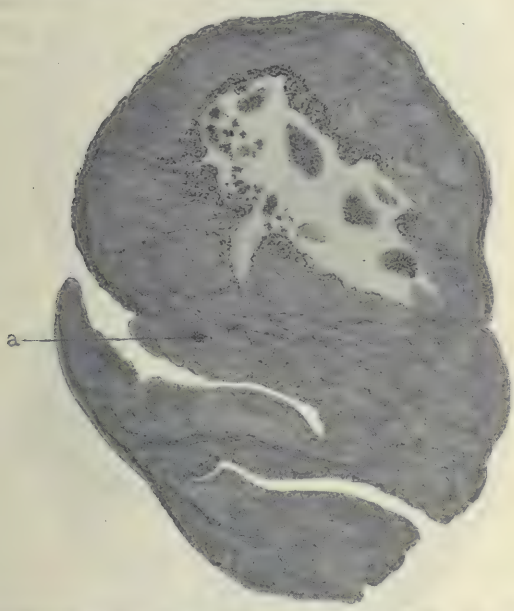
It is my interest in the suggestiveness of this case which induces me to bring it before you for consideration. Incidentally it illustrates one point which I have attempted to emphasize on many occasions, and that is the desirability of examining microscopically

[1] Zeitsch. f. klin. Med., 1896, No. 30, p. 529.
[2] Centralbl. f. Laryngologie, 1895, No. 11, p. 901; Baumgarten's Jahresbericht, No. 10, p. 454.

absolutely all tissue removed from the nose and throat in the routine of either hospital or private practice.

This case was a boy, aged twelve years, who came into the clinic of the Manhattan Eye and Ear Hospital, in the service of Dr. Lewis A. Coffin, for enlarged tonsils. They were cut out by Dr. W. N. Hubbard, one of the assistant surgeons, and the boy went on his way rejoicing, was well a month later, and still remains so, no metastasis having as yet shown itself.[1]

FIG. 1.



Camera lucida drawing of a section of a tonsil, showing under low power an abscess cavity containing masses of actinomyces. At *a* is seen the beginnimg of the growth of a colony in one of the lymph nodes. There is a larger number of lymph nodes than usual in tonsillar hypertrophy.

In the routine of the clinic these tonsils were put in formalin and later in alcohol, embedded in celloidin, cut in sections, and stained in hæmatoxylin-eosin. Subsequently the whole tonsil was sectioned, but only the one cavity was found. With the various microscopic appearances of that we are here concerned.

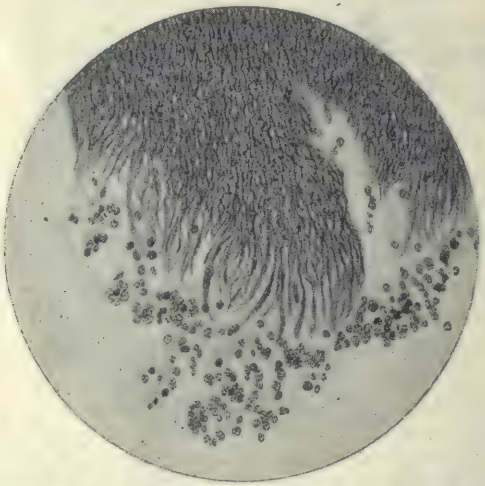
In Fig. 1 it will be seen the section traverses the whole tonsil covered with the usual striated squamous epithelium, with little or no keratosis. What is apparently an abscess cavity first attracts attention. It occupies a comparatively large area in the tonsil. In its cavity are seen the peculiar striated kernels which have at their

[1] I am unable to conjecture whether Ruge's cases were actinomycosis or not. In view of the variations in the toxicity of the different members of the group with the same morphology and, indeed, from the clinical histories of such cases, excision of a focus, even when only moderately complete, frequently prevents recurrence.

centre a blurred appearance and a yellowish tinge at the surface, taking the hæmatoxylin stain very faintly. A closer examination reveals the striations more marked at the edges. (The artist has drawn them somewhat schematically in this figure.) They are seen not only free in the cavity, but less distinctly along its walls, the granular masses making the picture indistinct.

Under a higher power there is seen in Fig. 2 the edge of one of these striated clumps and the peculiar branching, club-shaped rays of the actinomyces group appear, and through the blur and granulation of the interior of the clump one can make out the lace network, which is so characteristic. Around the ends of the ray or terminal filaments, which are variously described as loops and club-shaped

Fig. 2.

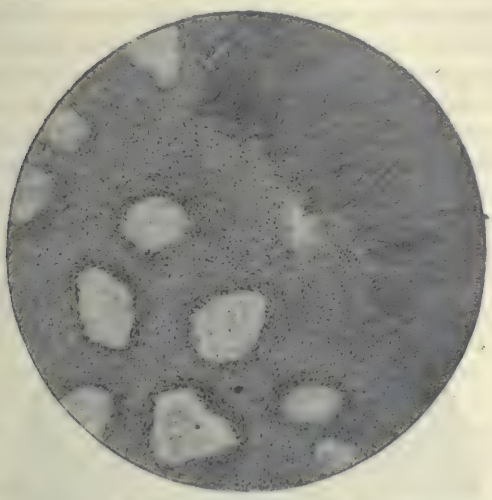


Camera lucida drawing under high power of the edge of one of the masses of actinomyces lying in the abscess cavity. The drawing does not give very accurately the "granulation" of the mass.

ends, are to be seen groups of much swollen leukocytes whose nuclei are granular or fragmented. When we come to examine the edge of the cavity we find that it is lined with a very greatly proliferated epithelium. In Fig. 3 it is seen that this proliferation differs markedly from that seen in crypts filled with the leptothrix. There is here no appearance of keratosis, but the fringe of epithelium is faint and very deep, enclosing islands of connective tissue. The nuclei of the epithelial cells are also fragmented. It has the appearance of the epithelium around an old syphilitic or lupoid ulcer. The ends of the actinomyces are pointed directly into the epithelium and invading it, apparently, as it breaks down by granular degeneration. Yet evidently the epithelium continues to proliferate under some stimulus, encroaching upon and surrounding islands of connective tissue,

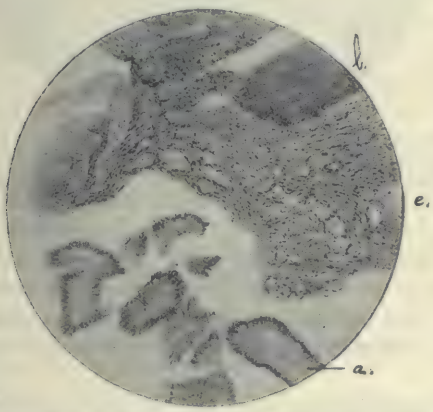
which doubtless at first contained round lymph cells. These apparently gave way first to the "granulation" process, to which the reticulum is also succumbing.

FIG. 3.



Camera lucida drawing under high power, showing the hyperplasia of the epithelium of crypt and the "granulation" due to the influence of the adjacent clump of actinomyces.

FIG. 4.



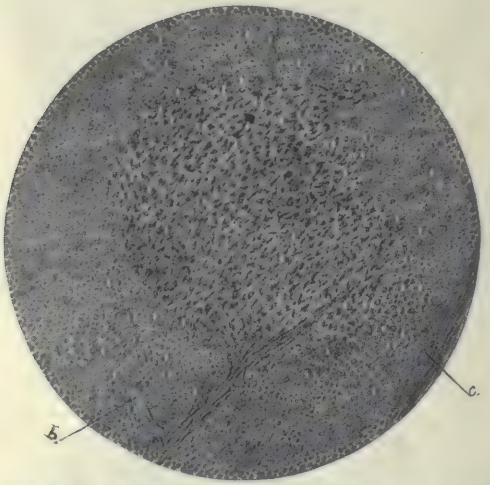
Proliferation of the epithelium of the crypt. The degeneration and the granular condition of the cells renders the epithelium atypical and indistinct. *a.* Actinomyces clumps. *e.* Epithelium. *l.* Lymphoid tissue.

It is apparent therefore that we have here the infecting germ lodged in a tonsillar crypt. After a longer or shorter time it began to multiply and excrete a toxin which, while it stimulates the proliferation of the bordering epithelium, gradually leads to its disintegra-

tion at the surface. The cavity of the crypt is thus painlessly enlarged, as there is no pressure, and the epithelium encroaches on the subjacent tissue. It is regularly the history of these actinomycotic abscesses wherever they form that they produce no pain. Neither do they form much pus, and the infection is not a mixed one. It is safe to believe that this proliferation of the epithelium has some influence in keeping the actinomyces from invading the subjacent lymphoid tissue, and we may thus understand why, without an abrasion, skin infection is such a rare occurrence.

In the warmth and moisture of a tonsillar crypt in this case this was an insufficient protection, for if you will refer again to Fig. 1 you will perceive that the lymph nodes are more swollen and

FIG. 5.



Camera lucida drawing under high power of the colony seen at *a* in the low-power drawing of Fig. 1. The fragmentation and breaking down of the lymph cells around the bundle of mycelial threads is very evident. *b*. Branching of the filaments. *c*. Edge of the lymph node.

prominent in the section than usual, and that in one of them at a distance from the affected crypt there is seen at *a* an area small in size. Under the microscope it has the same blurring and the same faint yellowish tinge with the low power as do the clumps in the crypt.

When we examine this spot with a high power (Fig. 5) we see some parallel threads, without joints, but with a tendency to branch. You will note that at *b* there is no fragmentation at the ends of the small branch, but at the terminal points of the larger and chief bundle you will note a destructive fragmentation of the nuclear material of the lymph cells. Elsewhere in the node these are normal.

A great deal has been written both as to the disease actino-

mycosis in man and in cattle, and as to the morphology and classification of the organism with which the disease is associated.[1] While it is said by Israel that von Langenbeck observed the disease in 1845, and various others from time to time referred to the condition, its nature was not recognized until the rise of modern bacteriology. Since then various names have been suggested for the organism. It has been called a streptothrix, cladothrix, oöspora, but the name actinomyces, suggested by the botanist Harz, has remained on the whole the one usually employed. MacCallum and others have used the affix asteroides to designate the appearance of the clumps, or asterisk-like "drusen." It was Bollinger[2] who first observed, in 1876, a microphyte in the lumps which are so often seen about the jaws of cattle, and referred the organism to Harz for a name. In the same year Israel described the disease in man,[3] but did not connect it with the cattle affection. This was pointed out by Ponfick[4] in 1879. Classified at first among the fungi, it was supposed to be insusceptible of artificial culture. Although Johne failed in 1882,[5] a more successful attempt was made by Boström in 1885.[6]

Since then numerous and varied experiences with its life forms and different culture media have led to much discussion.[7]

I do not propose—indeed I am not able—to refer to all the variations in the pleomorphism of the organism. Suffice it to say that it appears under various conditions as a streptothrix or streptobacillus, long threads sometimes straight, sometimes in loops, sometimes in such short rods that they resemble cocci. Club-shaped branching appearances are shown in my drawings. As I understand it, the question of spore formation has not been fully settled. Mertens[8] declares that their presence has not been proven, while the contrary is asserted by Berard and Nicolas (*ibid.*).

It seems the drift of recent opinion that "a number of different micro-organisms may cause the typical disease picture."[9] Not only is this the opinion of Dr. W. T. Howard, but more recently[10] we are to infer from the researches of the same observer, supported by the testimony of others, that there are varieties, indistinguishable

[1] A reference to the indices of the Centralblatt f. Bakteriologie, the Centralblatt f. Laryngologie, and Baumgarten's Jahresbericht will put anyone on the track of practically all that has been written on the subject in twenty-five years.

[2] Centralblatt f. d. med. Wissensch., 1877, No. 27.

[3] Virchow's Archiv, Bd. lxxiv.

[4] Berl. klin. Woch., 1879, p. 347.

[5] Deutsche Zeitsch. f. Thiermed., 1882, Bd. vii.

[6] Berl. klin. Woch., No. 1.

[7] The latest contribution I have seen being the article on the subject by Lignieres and Spitz, under the title "Contribution à l'étude à la classification et à la nomenclature des affections connues sous le nom d'actinomycose." Centralbl. f. Bakt., I. Abt. Originale, 1904, No. 3, Bd. xxxv.

[8] Centralbl. f. Bakt., 1901, No. 16, Bd. xxix.

[9] Howard. Actinomycosis of the Central Nervous System, Journal of Medical Research May, 1903.

[10] Ibid., January, 1904.

morphologically from pathogenic forms, which are entirely harmless and non-pathogenic in animals, Howard having found such fungi growing in various samples of vaccine.[1]

As yet it remains undecided whether these varieties can be distinguished by culture methods, and at present, so far as I know, observation of inoculation of animals and a study by culture methods of cases occurring in man furnish the most promising fields of differentiation. It is only fair to say that so recent a writer as Mertens[2] agrees with the earlier statements of Pfeiffer that the division of actinomyces even into two varieties seems unwarranted, but it would seem from the work of Silberschmidt (quoted by Howard) and Lignières and Spitz that this opinion is now untenable, Howard quoting Lachner-Sandoval to the effect that there are as many as twenty-five varieties of ray fungi.

As to the tinctorial reactions: "Mycelium and spores stain by Gram and retain carbol-fuchsin after treating with 20 per cent. sulphuric acid." "In sections stained with hæmatoxylin or methylene blue the colonies are finely granular, and stain homogeneously with the blue stain" (Howard).[3] On the contrary, MacCallum[4] says: "The staining is not regular or homogeneous, and one frequently finds clear unstained areas, almost like spores in some bacilli, or, on the other hand and more commonly, only granular bodies along the course of the filaments take the stain, so that the organism looks like a dotted line, sometimes with a faint outline on each side of the row of dots. These fine grains are irregular in form and do not suggest spores."

Other observers also differ in so far as they look upon some of the granules as spores or cocci forms or fragments of degeneration.

A very much more interesting and directly suggestive part of the subject is the conclusion toward which a study of its morphology and its culture has led many observers as to its classification and its affinities to other organisms. Some of its pathogenic characteristics, as we shall see later, are also, to say the least, very suggestive in this respect.

To quote again from MacCallum: "The organisms show affinities on the one hand with the bacteria and on the other with the fungi. . . . Their size approaches more nearly that of the bacteria than that of most fungi, and they stand nearer to the bacteria than to the fungi from the fact that their filaments do not, as in the fungi, consist of tubules with doubly contoured wall and divided into segments by septa. They resemble the fungi, how-

[1] It is quite possible that Ruge's cases were really the actinomyces which had failed to penetrate the tissues, owing to their feeble toxicity toward their hosts. In my own case, though growing in a lymph node at one place, the organism may have been but feebly pathogenic.

[2] Loc. cit.

[3] Loc. cit.

[4] Centralbl. f. Bakt. Originale, 1902, No. 12, Bd. xxxi.

ever, in being branched structures which produce under certain conditions fine conidia on their terminal filaments."

We may omit here any extended reference to its affinities morphologically with the Klebs-Loeffler diphtheria bacillus. The subject has received some attention from Silberschmidt[1] and others.

A much more interesting subject for consideration is its relationship to the tubercle bacillus. As long ago as 1888 Metschnikoff drew attention to the variations in the morphology of the tubercle bacillus, and Czaplewski still further elaborated the subject in 1891. Metschnikoff declared that the tubercle bacillus was not the final stage, but represented a condition in the developing cycle of a thread-like bacterium. He showed the branching of the bacillus and the bud-like projections sometimes seen even in human tuberculous sputum. Mafucci demonstrated the same appearances more often seen in fowl tuberculosis. Fischl, in 1893, showed that these forms occasionally occurred in pure cultures, and seems to have been the first to call attention to the resemblance of the bacillus in this form to the actinomyces. A. Coppen Jones,[2] from whose work I have quoted the above, in 1895 pointed out characteristics common to both the organisms, and the details are beautifully shown in his plates. Pettersson[3] in 1899 drew attention to the culture affinities of the acid-resisting bacilli, and more recently Abbott and Gildersleeve[4] have again returned to the subject and remarked upon the "actinomyces-like development of some of the acid-resisting bacilli." It must be remembered that, besides various modifications in the pathogeny of the tubercle bacillus itself, the human, the bovine, the fowl, the fish, the turtle tubercle bacillus, there are the morphologically and in cultures closely allied grass, hay, and butter bacillus, which have no pathogenic properties at all, though the above authors have shown a slight amount of tissue change occurring when they are injected. Indeed, so far as pathogenesis to man is concerned, we have in the group a steadily progressive series of organisms from the harmless butter bacillus of Rabinowitsch, through the turtle and fish bacilli,[5] to the bovine and human bacilli, concerning the mutual virulence of which war has lately been waging

We know with much less accuracy the interrelationship, as to pathogenesis, of the various members of the actinomyces group of bacilli, but we have some reason to believe that a similar series will be revealed in this family of organisms. Abbott and Gildersleeve have shown that the grass and hay bacilli injected in animals form in clumps with granular leukocytes around them in a manner similar though not identical with the actinomyces clumps.

[1] Deutsche med. Woch., 1901, No. 47.
[2] Centralbl. f. Bakt., Nos. 1 and 2, Bd. xvii.
[3] Berlin. klin. Woch., 1899, No. 26.
[4] Centralbl. f. Bakt. Originale, 1902, 1st Abt., Bd. xxxi.
[5] Friedmann, Centralbl. f. Bakt. Originale, 1903, Nos. 7 and 8, Bd. xxxiv.

Finally, the actinomyces is essentially an aerobic organism, and it has been shown by Coppen Jones, most recently supported by Wollbach and Ernst,[1] that the tubercle bacillus growing on a favorable medium shows more frequently the branched forms when the access of oxygen to the culture is most free. Whether the ray-fungus, on the contrary, shows more forms analogous to the usual forms of the tubercle bacillus when its culture medium is poor and the access of oxygen limited, I am unable to ascertain. Suffice it to say, as to classification, that generically these two microphytes seem closely related and stand between the lower and higher forms of microbic life. To use expressions current in German literature, the actinomyces is a "facultativ-parasite," the tubercle bacillus a "facultativ-saprophyte," *i. e.*, they both grow, though with difficulty, the former within and the latter without the animal body. Conversely the actinomyces grows readily on plants and the tubercle bacillus readily in animals.

It is necessary to say a word of the occurrence of actinomyces in nature and of the source whence man derives the organism when infected. It was formerly surmised, after Ponfick had shown the disease in man was identical with the more common infection in cattle, that man derived it direct from the latter, and, as usual, it was claimed in Germany that American cattle were more commonly affected than the beasts of the Rhineland. As a matter of fact, however, the majority of cases in which it was possible to trace the infection from an external source have shown that the organism was carried into the tissues, usually of the mouth, but rarely of the skin,[2] by the intrusion of foreign bodies, such as stalks and ears of grain or pieces of wood. Indeed, grain kernels have been found between the teeth of cattle, on which actinomyces were growing. It has been shown by Berestnew that straw dampened and placed in a thermostat will frequently, after a week or two and the removal of other more quickly growing colonies, show the presence of the actinomyces. The organism grows in the comparatively large air cavities and channels of the straw stems, doubtless because it is left there unmolested, yet exposed to the air a sufficiently long time to fructify and draw sustenance from the plant cells. It would seem therefore a matter of considerable doubt if the germ enters the system of man very frequently with the meat of cattle, though the number of cases of primary intestinal or peritoneal lesions might argue in favor of this method of infection. At the most it is a rare affection in man in any situation.

In discussing the port of entry of the organism we find another field in which something may be gleaned of interest in the wider topic of human tuberculosis. It is perfectly apparent, in looking

[1] Journal of Medical Research, December, 1903.
[2] Von Bergmann, Berl. klin. Woch., 1904, No. 1.

through the abstracts of cases reported in laryngological literature, that reports in the vast majority of the cases refer to lesions about the jaws and necks, many of them proved to be connected directly with a carious tooth cavity. Naturally the criticism is suggested that laryngological literature is hardly the place to seek this sort of evidence of the comparative frequency of the location of the lesion. We will therefore turn to bacteriological literature.

In 1887 Bollinger[1] stated that Moosbrugger, in collecting reports of ninety cases, found that in 10 per cent. no port of invasion could be made out, but in the majority of cases the mouth and pharynx seemed to be the starting point.

On glancing at the cases referred to in the *Centralblatt für Bakteriologie* since 1887 a tally, which may not be absolutely correct, shows that the primary lesion was situated around, or the port of entry of the infection could be traced to:

The neck or jaws, mouth or pharynx	72	cases.
Primary lesion in abdomen or its viscera	18	"
" " thorax walls, lungs, or pleuræ	21	"
" " brain	3	"
" " skin	3	"
Total	117	"

In 1899 Rütmeyer,[2] from a review of the literature surmised that the port of entry was the mouth and pharynx in 50 per cent. of the cases; lungs, 20 per cent.; intestines, 15 per cent. Of the 113 cases studied by Miller[3] in the same year, 53 were referred to the regions of the mouth and pharynx.

In a very large number of cases the tissue changes can be traced directly to a carious tooth cavity. In others they stand in such relation to a carious tooth that the port of entry can hardly be doubted. It is true many infections occur about the jaws of people with healthy teeth, but in those of untidy habits the crevices between the teeth, as we have seen in cattle, would furnish a sheltered nook for the slowly noxious effect on the epithelium. A careful analysis of the cases will show that the larger number of cases of lesions about the jaws present a lesion about the *lower* jaw, the lesions about the upper jaw being in a marked minority. We can scarcely explain this, when we have such strong evidence that the teeth are at fault, except on the assumption that the force of gravity drains the tooth cavities and normal crevices between the teeth of the upper jaw. While of course an imperfect protection, it would be sufficient to account for the greater preponderance of apparent infection through the teeth of the lower jaw. I desire to lay emphasis on this influence of gravity on the portals of infection, as I shall return to the subject when we come to consider the bearing of the

[1] Centralblatt f. Bakteriologie, 1888, p. 501.
[2] Berl. klin. Woch., 1889, Nos. 3 and 4.
[3] Die Mikro-organismen der Mundhöhle, Ed. 1889.

evidence of this rarer form of bacterial infection upon the more important subject of tuberculous infection.

Evidence of the influence of gravity is still further presented in the rarity of infection with actinomyces through the skin. This has occurred, but so far as I know the proof of its actual occurrence has, with one exception, always been associated with the entrance of a foreign body. In 1895 Hummel,[1] in a search of all literature, found but twelve cases, to which he added one, in which it seemed that the organism entered the tissues in a breach made by a foreign body, the grain of a cereal, in all but two cases. The case related by von Bergmann, in which actinomyces infection followed the kick of a horse, may be placed in the same category, but here the solution of continuity was in the skin, while in the other cases referred to the mucous membranes were pierced in the majority of the reports. While therefore we have good reason to believe that man, like cattle, receives his actinomyces infection in his food on grain and vegetables rather than in his animal food, it seems probable that the organism must either be carried at once beneath the epithelium by the intrusion of a foreign body, or it must find some lurking-place where it may remain in contact with the epithelium for a long space of time under the influence of warmth and dampness.

The query arises, Could it under such circumstances pass through the intact squamous epithelium? If you will glance at Figs. 3 and 4, you will see what effect it is exerting on such epithelium, while the evidence of Fig. 5 will convince you that somewhere in this region of the tonsil it has passed the epithelial barriers. In support of this evidence of a microbe allied to the tubercle bacillus being able to pierce squamous epithelium even of the skin, when placed under proper conditions of warmth and dampness, I may cite the instances referred to by von Bergmann where actinomyces caused lesions in the crevices of old scars, as in those from breast operations, too long after operation, presumably aseptic, to think of entrance at the time of the skin cutting. This might be a profitable point to clear up by animal experimentation, making artificial skin pockets and placing in them actinomyces of known virulence.

It is difficult to say how the chemistry of the gastrointestinal tract affects the actinomyces. It is of course certain, considering its prevalence on plants, that it is frequently carried into the stomach of man with his food, and still more frequently into the gastro-intestinal tract of cattle.[2] I am not acquainted with any investigations which show the relative frequency of actinomyces disease of

[1] Centralbl. f. Bakt., 1895, No. 2, p. 180.

[2] In this, however, I may be mistaken, for Mari (Centralbl. f. Bakt., 1892, Bd. ii. p. 854) examined for actinomycosis 42,230 cattle and found the lesion in 1030, or 0.02½ per cent. of the total number. Of these 1030 cases the lesion was about the lips in 621, or about 60 per cent., which as we have seen is not far from the ratio about the mouth in man. Berg (Centralbl. f. Bakt., 1899, 2te Abt., Bd. xxvi. p. 231) is said to have examined 400,000 (?) sheep and found the lesion only in three cases, and these about the mouth.

the abdominal organs of cattle. I suspect, from general laws, that such lesions are relatively rarer in cattle than in man. As we have seen, abdominal actinomycosis stands next in frequency to that of the lungs in man. It is very probable that many cases of apparent primary pulmonary actinomycosis are secondary to lesions higher up which have not been recognized, but whatever may be the truth in regard to tuberculosis, I think we can hardly thus explain the cases of actinomycosis of the abdominal cavity. In reference to this point Grill,[1] who in 1895 collected 107 reports of cases of intestinal actinomycosis, considered the germs too big to be carried by lymph channels, a statement which will hardly stand criticism to-day, though it would seem that *something* hinders them from travelling much by the lymph channels. It seems likely they are carried chiefly by bloodvessels.[2] Although no part of the intestinal tract seems to be proof against their absorption, most of the cases proceed from the cæcum and the vermiform appendix. I have noted three reports of appendicitis due to it. This would be a locality where a germ would lie longest undisturbed. I wish to draw attention to the rarity with which not only actinomycosis but tuberculosis seems to have its origin from œsophageal absorption, which can scarcely be accounted for in any other way than by the rapidity with which the infecting material passes the surface. The same may be said in regard to nasal infection. The constant drip of secretions from the upper regions of the nose tends to wash rapidly away any germs deposited in the lower respiratory channels of the nose. The sluggishness of the lower bowel gives an opportunity for the absorption of bacterial ptomaines and of the bacteria themselves, which is not presented by the upper digestive tract, due doubtless in large measure to its active peristalsis. Within the tissues we have an instance of the opportunity which stasis offers the tubercle bacillus in the preponderance of primary apical lesions of the lungs over that of other pulmonary localities.

From the consideration of these *a priori* reasons, supported to some extent by more direct evidence, the inference has been that the faucial tonsil, standing at the very forks where the breathway and foodway meet, existing normally in the form of folds and pits, but these pockets exaggerated enormously in hypertrophic disease, is the spot par excellence whence all sorts of pathogenic bacteria would start on their maleficent journey through the blood and lymph channels of the human body. From this alone we might expect to find there protective influences which prevent the annihilation of the race. More than forty years ago Virchow declared it to be

[1] Centralbl. f. Bakt., 1895, 2, p. 181.

[2] This suggestion is supported by the description of the post-mortem findings in a case reported by Lesin (Centralbl. f. Laryng., 1895, No. 11, p. 901). It is probable, as I have said, that in this case the port of entry was the tonsil, since the primary lesion was in this vicinity. There was much infiltration around a large bloodvessel in the neck, and the case terminated fatally from cerebral involvement.

entirely incomprehensible why the tonsils possess immunity in spite of the fact that they are lymphatic organs. We have learned much since then, but in spite of the horde of names recently poured into the already gorged channels of pathology by the recent researches in immunity we all recognize that we know comparatively little of protective influences. We only know they are multitudinous, and gathering them together into one word, "immunity," is convenient, but it has been very misleading. I think Figs. 3 and 4 show that the squamous epithelium lining the crypts of the tonsils is one of these protective agents against the invasion of the actinomyces. Now I have hinted that forces which keep the bacteria on the move, dripping secretions, waving cilia, intestinal peristalsis, gravity, must also be placed in the category of the defenders of the animal organism against the invasion of the pathogenic germs, these being more important in the production of that relative local immunity to which Virchow so often referred. That this keeping the germs on the move plays no inconsiderable part in slowly growing germs like the actinomyces and the tubercle bacillus, preventing them from penetrating the epithelium, we may readily believe if we are warranted, as seems the case with the actinomyces, in thinking that their toxins play a part in opening a port to their intrusion.

But if a tooth cavity will lodge a slow-growing germ long enough why will not a tonsillar crypt? And if so, why does not actinomycosis of the tonsil more frequently occur?[1]

One reason is doubtless, as we have seen, the resistance of the epithelium. Such protection does not obtain in a carious tooth cavity. There are other protective influences which are associated with the tonsil, and not with dental caries; these are gravity, mobility, exosmosis.

In speaking above of the drip of secretions rendering the upper meatuses of the nasal cavity relatively aseptic and the inferior meatus less foul than we would expect, I have intended to introduce the consideration of a factor which must obtain on all moist surfaces of the airway and foodway to some extent. The excretion of fluids, osmosis from within outward, whether through glandular or surface epithelium, must be a process which tends to wash out or keep out the pervasive germ. In the absence of the waving cilia of the epithelium, which works against gravity only in the dependent cavities, such as the accessory nasal sinuses and the pulmonary tract, gravity carries the secretions and their bacterial contents downward. These secretions themselves are apparently to some extent inimical to the existence or rather to the continued virulence

[1] The suggestion of Westenhoeffer (Berliner klin. Wochenschrift, 1904, No. 7) that the most frequent port of entry of the tubercle bacillus in infancy is through the break in the epithelium of the gums at the time of dentition, does not suffice in accounting for the usual route of entry, yet both in this breach and in the cavities of carious teeth the bacillus tuberculosis may find that opportunity which seems to furnish the most frequent access to the actinomyces.

of pathogenic germs, but the gastric secretions annihilate many of the bacteria carried into the stomach. In addition to exosmosis, which, since it has not been demonstrated for the tonsillar crypts, we may for the moment ignore, the motion imparted to the tonsillar structure by muscular action in deglutition, as in intestinal peristalsis, is sufficiently evident. The unskilled examiner is fully aware how, when he nervously forces down the tongue, the large tonsillar crypts gape in the reflex gagging of the patient. In the act of deglutition the passage of fluids and masticated solids across the mouths of gaping tonsillar follicles must tend to suck and siphon out the contents of the crypts and lacunæ. It is true of course that the configuration of some of these is such that they are thus incompletely emptied, but the conception that these cavities are the constant and crowded lurking-places of all sorts of bacterial life has been very much exaggerated. I have stained many hundred sections of tonsils to demonstrate in them the presence of bacteria. Not only have I failed in all but an insignificant number of cases to detect any bacterial forms beneath the deeper layers of the epithelium, but I have been much more puzzled to account for the comparatively few crypts which show any considerable number of bacteria outside of the epithelial wall. In very sparse numbers, it is true, with diligent search, they may be found if properly stained. Here and there one or possibly two and three cocci may be seen lodged in a nook under the upturned edge of an epithelial cell. This is the general rule, but it occasionally happens that vast numbers may be seen in a crypt, in striking contrast to neighboring lacunæ. I can only conclude that the complete or partial closure or the valve-like action of the mouth of the crypt has prevented the cleansing of the cavity in the manner I have described. These are the crypts recognized clinically by the white, cheesy masses in them, but they are insignificant in number when compared to the total number of recesses. The mechanism which keeps the latter free of visible solid matter is also a very efficient scavenger of bacteria.

Nevertheless there are enough germs in contact with the epithelium for a sufficient length of time to force ingress were they endowed with powers of penetration, but usually these bacteria are either non-pathogenic, or if they are pyogenic cocci they are non-virulent toward their host, as long at least as the latter's systemic repelling forces are in proper order. In such a swarm of microphytes as I have just alluded to a slow-growing tubercle bacillus or an actinomyces would ordinarily have an unsuccessful struggle for existence. We are fully warranted in believing that thus non-pathogenic parasitic bacteria exert at the so-called portals of infection a protective influence over the animal organism, a presumption which under other phases is a familiar and well-accepted belief.

But why is it that under such conditions of abundant bacterial life in a crypt—the cavity fairly gorged with microphytes—we can

detect none beneath the epithelium? We are familiar with the experiments of Goodale and Hendelsohn which have shown that minute carmine particles injected into the crypts or even simply blown on the surface readily pass through the epithelial barriers. Pirera[1] performed similar but not very convincing experiments with the bacillus prodigiosus, but his results are so diametrically opposite to what we observe in actual occurrence of plugged crypts that I am not disposed to accept his conclusions that bacteria also pass through the epithelium.

It is true that in acute inflammation staphylococci, streptococci, diphtheria bacilli are to be seen in the subepithelial structure. It is exceedingly doubtful if at such times we can suppose that other slow-growing forms (*e. g.*, tubercle bacilli) survive in the struggle for existence in the crypts and live to enter the tissues. In the quiescent tonsil the picture is quite a different one, and if we are to suppose that it is then the tubercle bacillus enters, it evidently differs from the other bacterial contents of the crypt.

Distrusting experiments in which a mass of powdered substance in exceptional fashion was deposited in the crypts and blown on the surface of tonsils, I studied numerous unstained sections. I sent to the dusty city of Pittsburg, and through the great kindness of Dr. Day and Dr. Jackson I was able to secure the tonsils of some of its citizens, exposed for years to the deposit of coal-dust particles. There can be no doubt that dust thus deposited in the usual way follows the same course as that deposited in the experiments of Goodale and Hendelsohn. It seems therefore that the dust passes, but cocci and bacilli of the same or smaller dimensions do not pass into the quiescent tonsil. At least if they pass they do so in such greatly reduced numbers that it leaves the contrast to the behavior of dust particles a striking and unexplained phenomenon. There are certain cases which are very rare, but which we nevertheless occasionally see in the clinics, in which are to be observed fine white points scattered throughout the tonsil itself, which are not plugged crypts. Microscopic examination will frequently show these to be tiny abscesses of the lymphoid tissue, small cavities gorged with cocci. Further examination shows that numerous cocci may be seen elsewhere in the lymph channels of the tonsil at a considerable distance from these foci.

Without pain or fever or constitutional disturbance of any kind it is evident that something has occurred here which has permitted the entrance of the surface bacteria. The cases I have seen have been in children with a phthisical family history, and the thought suggested itself to me that these individuals may also absorb dust more readily than the numerous other cases I have studied in which I made no selection. I was fortunate after some time to receive

[1] Archivii Italiani di Laryngologia, Fasc. 2, 1900.

from Pittsburg tonsils cut from children with a known marked tuberculous family history and from cases of phthisis pulmonalis. Neither in these nor in the lymphoid abscess cases could I make out any greater amount of dust passing.

We are free to infer that nature in the process of repelling the invasion of morbific germs has in the process of evolution accumulated around these diverticula of the tonsils, as elsewhere in the alimentary tube, those cells of the organism which supply the antibodies to the tissue juices, and that they are held in place by the mesh of lymph channels which may be too small at places to transmit some germs (*e. g.*, the actinomyces). This at present is a familiar conception, but from the study of the problem as indicated above we seem to be also in the presence of some wonderful mechanism of nature, evolved through æons of time, and established at the portals of infection, by which harmelss atoms glide through the stomata of cells, or their interstices, which close at the approach of the microbic enemy. When that mechanism is in perfect working order we may conjecture that the toxin of the actinomyces, the tuberculin of its more deadly cousin, is powerless to overcome it. These germs may enter immediately the undefended portals of the "predisposed," or they may lurk at the door until, in an unguarded moment—at the moment of exhaustion from illness, starvation, or other systemic disturbance—the toxin opens the path and the microphyte passes the first barrier. I do not know what part, if any, the epithelium of the tonsils may play in the production of antibacterial ferments. It is supposed by some observers that the intestinal epithelium is an important tissue in its manufacture. If so, the problem in the crypts of the tonsils may also be a chemical one, but it seems to me the attention of observers has been too intently fixed upon what follows after the microbe has passed the epithelial barrier. It is the error we are constantly falling into, the exaggeration of a single factor in the body's fight against disease. We forget that the etiology of disease is a complex problem.

I do not know how much resistance is offered by the normal epithelium to the tubercle bacillus. I have definitely shown that under morbid conditions it may pass freely through squamous epithelium.[1] You will see by a glance at Figs. 3 and 4 how the tonsillar epithelium reacts to the presence of the adjacent actinomyces. I am sure you will be struck by the resemblance to the epithelium around ulcers, especially of a syphilitic or tuberculous nature. Now after the actinomyces has passed at some unguarded gate you see how its toxin has fragmented the nuclei of the lymph cells in Fig. 5, and again we are reminded of the specific granulomata.

[1] See the plate attached to the paper on "Tuberculous Infection of the Lymphoid Tissue in the Pharynx, with some remarks on Laryngeal Infection," New York Medical Journal, September 26, 1896, read that year before the American Laryngological Association.

There is another curious analogy to syphilis at least. Van Niessen's[1] observation of the occurrence of a microphyte resembling the actinomyces in cases of syphilis has, so far as I know, received no support, but not only has the iodide of sodium a very favorable effect upon the lesions of actinomycosis, but solutions of comparatively weak strength ($\frac{1}{8}$ per cent.) retard and stronger ($\frac{1}{2}$ per cent.) solutions inhibit the growth of the actinomyces.

Whatever may subsequently be proven to be the virus of syphilis, we know the effect on cells under certain conditions of the virus of actinomyces and of the tubercle bacillus. What we have seen and what we are familiar with is the result of a destructive agent upon cell life. We know very much less accurately the biological processes which the toxin of these bacteria excite in the activity of the cells. The tuberculin evidently profoundly modifies their function. What it does in a chemical or biological way is shadowed forth in some of the terms in the recent observations on immunity, but how it affects them mechanically is entirely unknown. How the endothelium of the lymph channels may dilate or contract or become swollen we do not know, and yet that lies at the root of the problem of their carriage through the tissues. In this connection a recent remark of von Behring is suggestive:[2] "To scrofula I ascribe the alteration in the muscular coats of the blood-vessels brought about by T. B. infection, which finds an expression in excessive sensitiveness toward tuberculin, and which in general may be compared to the scrofulous diathesis of the older writers."

To pursue this subject farther would lead us too far from the portals of infection, which was the site of the activities in this unique case of actinomycosis of the tonsil.

REPORT OF A CASE OF RUPTURE OF AN ANEURYSM OF THE AORTA INTO THE LUNG, WITH SPONTANEOUS RECOVERY.

By N. S. Ferry, M.D.,
of Memphis, Tenn.

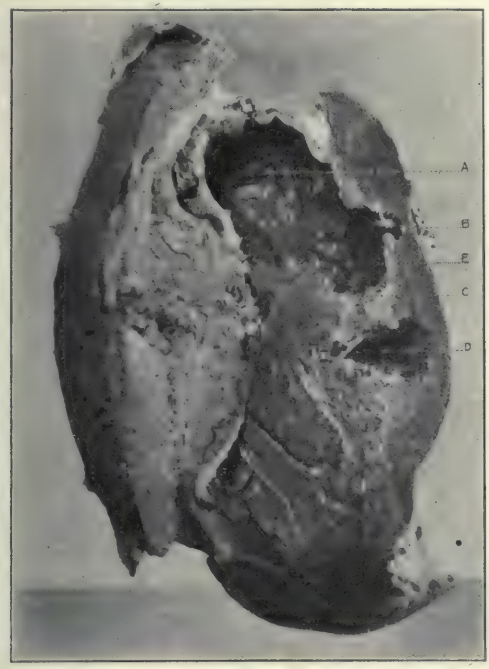
The following rare case occurred in the service of Dr. A. R. Defendorf, pathologist and assistant physician to the Connecticut Hospital for the Insane, with whom the writer had the pleasure of working during the summers of 1900 and 1901. The history of the case was kindly furnished by Dr. Defendorf.

The patient was a man of unknown personal history, except that he had had syphilis, suffered from organic dementia, the onset of which occurred at forty years of age, immediately following head

[1] Berl. klin. Woch., 1904, No. 4.

[2] Centralbl. f. Bakt., 1898, No. 2, Bd. xxiii.

injury. He was admitted to the Connecticut Hospital for the Insane three months later in a condition of pronounced excitement, which continued this time for two years. He was always in excellent physical health, and from forty-two years was successfully employed in the hospital, as he presented but a moderate degree of deterioration. At fifty-eight years (March 26, 1898) he suffered from a very profuse pulmonary hemorrhage, from which he rallied rapidly, but from this time, although physically robust and never complaining of ill-health, he discontinued work and spent his time lounging. At sixty years, February 17, 1900, without previous evident change, he was found dead in bed surrounded by a large pool of blood.



A. Upper. B. Lower. C. Point of entrance. D. Abscesses of wall.

The following is a description of the specimen in the laboratory of the Connecticut Hospital for the Insane:

The superior lobe of the left lung into which the rupture occurred is very dark in color and very firm to the touch, as if completely consolidated. On section the remainder of the lungs are found to be healthy. No signs of tuberculous or any other cavity formation.

The upper half of the superior lobe of the left lung is taken up by the aneurysmal sac "A," and is somewhat elongated, measuring 8 x 8 x 5 cm. As the lung was sectioned it appeared to occupy the space of about one-half of the lobe. At the lower end of the sac

there seems to be a dilatation forming a second sac, "E," measuring 3 x 3 x 2.5 cm. Immediately beneath this sac "E" is seen a cavity in the lung tissue "D," 4 x 3 x 1.5 cm. in size. This cavity "D" is situated in about the centre of the lobe, 9 cm. from the superior surface of the lobe and 1 cm. below the inferior wall of the aneurysm. The walls of this cavity are composed of healthy lung tissue, are very ragged, and give the appearance of having been torn apart but a short time previous. This cavity, which was discovered distended with clotted blood at the time of the autopsy, is found to communicate with the second sac "E" of the aneurysm by means of a small opening "C," through which the blunt end of a dissecting probe may be passed. The walls of the aneurysm proper are very much thickened and studded with necrotic areas varying in size from a small pea to that of a ten-cent piece, many of which are undergoing ulceration. The ulcers of the second sac "E" are very much thinner and do not contain necrotic areas similar to those found in the walls of the aneurysm itself. On the surface of the lung just over the second sac is seen a depression, "B," about 2.5 cm. in length and 1 cm. in width. On section at this point the tissue is found to be about 2 mm. in thickness. It is clearly seen that the sac approaches nearer the surface at this point than at any other. The tissue at this point is very hard, dense, and of a light color, and is composed mostly of scar tissue. It is attached directly to the pleura and appears to be the scar of some previous rupture. This theory is further borne out by the fact that the wall of the sac at the point "B" for a space of 5 cm. in distance is missing and its place is taken by the previously mentioned scar tissue. The first hemorrhage, which took place two years before the fatal hemorrhage, probably occurred through the rupture, and from some unknown cause healed of its own accord.

Beyond the lungs the aneurysm, which occupies the entire aorta for about 10 cm. in length, is fusiform in shape. The walls here are also studded with numerous areas of necrosis similar to those found in the sac within the lung.

After a fairly careful search through the literature, the rarity of this occurrence was made very apparent, as only a few cases were found where a patient had lived any length of time after a rupture of an aneurysm of the arota, and still more rare are those cases where the scar of the rupture was found. The eight cases found in the literature are of enough interest, I think, to warrant the publication of a short résumé of each.

Case I. (M. Howard Fussell, *Transactions of the College of Physicians*, Philadelphia, 1891, third series, vol. xiii. pp. 127–132. "Aneurysm of Aorta, with Healed Rupture and Recent Rupture.")—Patient, aged forty-six years, presented himself at the Medical Dispensary of the University of Pennsylvania, July 29, 1887. For two years under the care of Dr. George Dock. Complained of pain in left chest and back lasting for several months. Was put on a mix-

ture containing potassium iodide. On April 5, 1888, patient awoke at 3 o'clock with a salty taste in his mouth. Cough came on and he spat up about one pint of pure blood, frothy at first and afterward clotted. Was kept in bed and put on low diet. A note on the 30th: Sound, dark-clotted blood spat up yesterday with epistaxis.

August 19, 1891. Patient died suddenly after going to bed last night.

Autopsy Twenty-four Hours Post-mortem. On opening the cavity of the chest a considerable amount of serum exuded from the left side. All the organs were displaced to the right. Left lung was floated upward. Cavity filled with serum and blood. Aneurysmal sac began at the middle of the arch and continued to the bottom of it. The left lung was adherent to the sac, over an area of five by five inches. The adhesions were old and firm, and the lung was spread out in a thin layer over the adherent portion of the sac. The sac was empty. In some spots there were small recent clots, and one of these in the anterior part of the sac, where the lung was adherent, filled a round cavity, which proved to be a healed ulcer, the base of which was the lung. Farther back was another healed ulcer, which was half an inch in diameter. It was shallower than the other, but showed lung tissue at the bottom. One inch from the lower end of the sac, on its concavity, was a recent laceration one and one-half inches long, with irregular edges and somewhat S-shaped. This was the recent rupture which caused death.

The author remarked that the case was remarkable for the severe hemorrhage which did not prove fatal. This hemorrhage doubtless took place through the small ulcers over the adherent lung. The blood that was coughed up was frothy, and that lung showed changes after the hemorrhage.

Case II. (Wilks, *Transactions of the Pathological Society of London*, 1861, vol. xii. p. 71. "Aneurysm of the Aorta; Rupture into the Pericardium; Subsequent Closure by Inflammation.")—Male, aged sixty-two years, was admitted into Guy's Hospital under the care of Dr. Wilks, on December 6, 1860, suffering from all the symptoms of heart disease. There was considerable dyspnœa, slight yellowness of the skin, and dropsy of the legs. On listening to the chest a very slight and scarcely perceptible systolic bruit was heard over the neighborhood of the valve and limited to that spot; thus the nature of the cardiac lesion was not at first apparent. On the next visit two days afterward the man was found to have acute pericarditis, denoted by a loud to-and-fro rub over the base of the heart. The pericardial signs continued for some days, when they disappeared, giving place to the very indistinct systolic murmur at first heard. The original symptoms had increased and continued to grow gradually worse until death, January 6, 1861.

The pericardium on being incised was found to be closely adherent to the heart, but it was easily stripped off, showing that the inflam-

mation was recent; in fact, about three weeks old. At the base of the heart a small space was seen between the serous membranes, and in this was contained some clotted blood mixed with lymph. Here, also, the ascending aorta was seen bulging outward in the form of a small aneurysm, and in the centre of the aneurysm was a rent holding coagulum. "It was thus clear that this rupture had been the cause of the pericarditis which took place two days after the man's admission, and that the lymph then thrown out had prevented a further effusion of blood and a fatal hemorrhage." The aneurysm itself was about the size of a small egg, was situated in the ascending aorta, and projected forward so as to cause pressure on the pulmonary artery, which was the cause of the heart symptoms.

Case III. (Felix Semon, *Transactions of the Pathological Society of London*, 1876–1877, vol. xxvii. pp. 76–85. "A Case of Aneurysm of the Thoracic Aorta, with Repeated Perforations in the Œsophagus.")—Patient, aged forty years, male, came on October 31, 1876, into the hospital for disease of the throat. Complained of dyspnœa, which increased at every moment, and of temporary pains in the chest, which seemed to originate under the sternum at the height of about the fourth to the sixth vertebra, and to move from there to the back. Food seemed to remain for some time at the same height, at the place of said pain, before entering the stomach. Two months before his admission he had once had a fainting fit without any known reason, since which time the stoppage of food is said to have begun. The diagnosis was made of "aneurysm of the arch of the aorta of a considerable size, but nowhere reaching the chest wall." Patient began to grow worse, vomiting set in, and during the last few days a short, dry, distressing cough began.

Post-mortem Examination Made by Dr. Barrett. The arch of the aorta from the very beginning to the middle of the descending part was considerably enlarged. At the height of the fourth to the sixth vertebra was a nearly globular aneurysm of the size of a small orange. It was united to the œsophagus and vertebral column.

The wall of the aorta was much thinner than normal over the entire extent of the adhesions to the œsophagus. The anterior wall of the latter was perforated circularly at the height of the fifth vertebra. The opening was about the size of a silver dollar. In this opening appeared a thoroughly organized, conical, brownish-red thrombus of the size and shape of the first phalanx of the little finger, which originated from the uppermost part of the posterior wall of the aorta. Its surface is rough and torn. In the middle of the posterior wall of the aneurysm was found a recent small perforation in the œsophagus. The author thought that the presence of the large thrombus in the œsophagus proved that the first bleeding must have taken place some time previously, probably when the patient had his fainting fit, three months before admission, and from which he also dated the difficulty of swallowing. The trickling of

blood must have occurred by drops and through a small opening, so that the extravasated blood had time to coagulate and to prevent, by the formation of coagulations around the perforations, an enlargement of the latter.

CASE IV. (Case reported by Dr. C. Hubner at the Hospital San Juan de Dios, at Ramanga, Chili.)—L. A., aged fifty-two years, admitted to the hospital April 9, 1862, on account of asthma trouble. Patient appeared to be slightly dropsical. A short time before admission he had vomited about four pounds (pints) of blood without much coughing. Color of blood was pale red. I diagnosed case "hypertrophy of heart and aneurysm of aorta." He remained in the hospital a few weeks and was discharged on his own request.

On February 12, 1863, he was again admitted for the same trouble. Had vomited a large quantity of blood about fourteen days previous. The hemorrhage had entirely ceased after about thirty hours. He was suffering greatly from asthmatic trouble and had severe fits of choking. I again diagnosed case "aneurysm of aorta." Under treatment he improved, and on February 26th asked to be discharged, which was refused. On February 27th he suddenly began to cough, spat up about two pounds of blood, and died within ten minutes.

Autopsy. Aneurysm found over the upper portion of the left lung filled with a mass of clotted blood. Lung tuberculous. The autopsy led me to believe that the aneurysm had existed for a long time and had ruptured twice. When he threw up the large amount of blood the first time a rupture had occurred; when hemorrhage suddenly stopped the blood became clotted in a layer over the rupture, forming a pseudomembrane. We thus have a spontaneous healing of a rupture of an aneurysm of the aorta. The second rupture, which was quite open and not covered with clotted blood, was the cause of death. There was extensive necrosis and loss of the periosteum of the spine, caused by the continued and permanent pressure of the aneurysmal sac on the spine.

CASE V. (Surgeon F. R. Town, United States Army, Fort Sill, Indian Territory. *Reports of the Surgeon-General of the Army,* Washington, 1885, 1886, 1898. "Report of a Case of Double Rupture of an Aneurysm of the Ascending Aorta, with Survival of the Patient for Several Weeks Subsequent to the Primary Rupture; Final Result, Death.")—Patient, aged thirty-two years, Mexican by birth, appeared at sick call complaining of shortness of breath and inability to blow his instrument, a brass horn. Four days afterward he was seized in quarters with a sudden faintness and alarming prostration. He was seen immediately by Acting Assistant Surgeon J. L. Powell, who found an entire cessation of respiratory movement, a murmur over the right side of the thorax, and universal flatness on percussion, while the respiratory movements of the ribs on the left side were evidently increased. Marked pallor of the face and

skin prevailed and the pulse was extremely feeble. Patient improved until May 28th, when, as he was in the act of sitting down to dinner, sudden faintness came on and he vomited a large quantity of fresh arterial blood. At 9.30 P.M. a violent hemorrhage occurred from the mouth and nose, with an almost immediate fatal result.

Autopsy Thirteen Hours after Death. The right pleural cavity contained a large amount of disintegrated coagula and fluid blood, which had evidently extravasated some time prior to death. Considerable damage had resulted to the superficial parenchyma of the lung posteriorly, especially near its posterior border, through which the escaping fluid had effected an entrance from the descending aorta. The pleural surfaces were firmly adherent to the chest wall and also to the lung itself, along the external surface and base. These adhesions were old and had limited the amount of extravasation. "To their strength was probably due the temporary preservation of the patient's life by preventing the general diffusion of the escaping fluid throughout the pleural sac and the forcible compression of the lung into the apex of the thorax." About one inch and a quarter below the origin of the left subclavian artery a sacculated aneurysm of moderate size, with a large mouth, projected from the right of the descending aorta in front of the œsophagus. The aneurysmal pouch was oval, and from one to two inches in diameter. A circular ulceration through the sac, about three lines in diameter and immediately over the œsophagus, indicated the position of the fatal rupture. After a little search a second small opening through the sac nearer its mouth was found, which communicated to the right and behind the œsophagus directly with the extravasation within the right pleura. The sac contained a small amount of clot and was partially lined with a thin lamina of fibrin, which was believed to have occluded the passage to the right thorax.

CASE VI. (Theophilus Thompson, *London Medical Gazette*, 1840, vol. ii. p. 905. "A Case of Aneurysm Supposed to Have Opened into the Pericardium a Considerable Time Before Death.") —On July 21, 1839, the patient, a blacksmith, of strong, muscular frame, was found lying in bed, lips and ears slightly livid, skin perspiring, and countenance rather anxious. Complained of pain on the right side of the sternum, increased by full respiration. Right chest was prominent, especially over the third, fourth, and fifth ribs, where the sound elicited by percussion was dull, while the natural dulness of the cardiac region to the left of the sternum did not extend so far as usual. Physician concluded that the heart was enlarged and the aorta studded with ossified depositions." He could not satisfy himself whether there was aneurysm of that vessel. Twelve months previously the patient had been attacked with pain in the back and side, since which time he had suffered from palpitation, and had occasionally fainted at his work. On the following

September the patient became worse, and on the 19th he was found again confined to bed with great lividity of countenance and a very weak and rapid pulse. He was treated at that time and improved until the 29th, when, on getting up for stool, he became suddenly worse, stared wildly for a moment, uttered an exclamation, and fell back dead.

Post-mortem Examination. Pericardial sac filled with clot. Heart enlarged and flaccid. Aorta near its origin was dilated to more than twice its ordinary size. Inner membrane seemed to have lost its natural elasticity. No ossification. At the most dilated part of the aorta an opening was discovered, the edges of which were even as if cut with a knife. This was probably made in removing the heart, but at one end of the wound, two or three inches above the aortic valve, was a somewhat puckered opening, apparently produced by disease. On tracing this aperture it was found to communicate with a sac. This pouch, which was larger than an orange, was full of dense coagulum and lined with fibrinous layers. At its outer side, nearly on a level with the aortic valves, was a round smooth aperture, rather more than three-quarters of an inch in diameter, through which the blood appeared to have escaped into the cavity of the pericardium.

"It seems reasonable to conclude that in this case the pericardium had not only been thickened by inflammation at some distant period, but had also been affected with more recent inflammation up to the time of death."

The indication of great displacement of the heart at an earlier period, the roundness and smoothness of the opening into the pericardium, the great distention of that membrane, the increased firmness of its structure, the evidences of recent and progressive inflammation seem favorable to the opinion that the rupture of the aneurysm into the cavity of the pericardium had occurred a considerable time before the death of the patient.

Case VII. (Charles Murchison, "Diffuse Aneurysm of the Thoracic and Abdominal Aorta, Terminating in Chronic Peritonitis, with Copious Liquid Effusion.")—Patient, James D., aged forty-two years, on January 1, 1869, suddenly felt ill and then immediately became unconscious, remaining in this condition for an hour. Following this at the beginning of August the patient had a severe attack of pleurisy, without any strain or unusual exertion was suddenly taken with urgent vomiting, severe pain, and distention of abdomen and constipation. On September 4th the sickness recommenced and was attended by pain in the stomach, but less severe than on former occasions. On the 10th he became worse, and since then had great pain and vomited everything he swallowed. His bowels had been relaxed and shortly before his admission had passed a considerable quantity of semicoagulated blood. He gradually became worse, and died on the morning of the 23d. At the

post-mortem an aneurysm was found at the lower part of the thoracic and upper part of the abdominal aorta.

COMMENTS BY MURCHISON. On January 1st the aneurysm ruptured and caused syncope. On August 4th the aneurysm burst in a downward direction and, the blood pressing forward, the liver and the peritoneum caused chronic peritonitis.

CASE VIII. (Dr. Rhodes, *London Medical Times and Gazette*, 1863, vol. ii. p. 10. "Rupture of an Aneurysm into the Left Pleural Cavity; Death Three Days after the Supposed Time of Rupture.") —T. W., aged thirty-nine years, decorator, was admitted into St. Mary's Hospital on February 11th, with supposed effusion into left lung. One week ago he became suddenly faint and fell down insensible, in which state he remained two minutes. On recovery he felt considerable pain on the left side. Was supposed to have received some injury to ribs. On examination the whole of left side was found dull on percussion, but absence of breath sounds and vocal vibration. No pulsation in cardiac region, but the apex beat could be felt in the epigastrium and the heart sounds to the right of the xiphoid. Death on the 14th.

Autopsy. Left pleura was filled with dark-colored serum. Heart displaced. Large clot of blood measuring four pints was effused over surface of the lung. On removing this a sacculated aneurysm about the size of a small orange was found at the posterior part of the thoracic aorta just at its termination, which communicated with the pleura by an opening about the size of a quill. No trace of pleurisy found.

If any one situation is more favorable than another for the spontaneous recovery after the rupture of an aneurysm of the aorta, the lung seems to enjoy that distinction, probably accounted for by the better facilities offered for the rapid formation of a clot with which the rupture is blocked. A number of cases are recorded where the patient lived a few hours or perhaps a day or two after the rupture of an aneurysm into the lungs, pleural cavity, or pericardial sac, but these cannot be placed under the heads of recoveries.

PRIMARY TUBERCULOSIS OF THE BREAST.*

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(From the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst Foundation.)

WHEN the function of the breast is taken into account, one would expect mammary tuberculosis to be as frequent as genital tuberculosis. This is certainly not true. Among 300 gynecological cases

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Stratz[11] found 22 per cent. of tuberculosis; Martin had 10 in 287 cases, and Whitridge Williams reported that 8 per cent. of inflammatory adnexal disease was due to the tubercle bacillus.

Mammary tuberculosis is more rare. Bartsch[9] in 1901 could find but 65 undisputed cases in the literature. Probably 30 of these were primary. The primary form of genital tuberculosis has been open to doubt. Such pathologists as Klebs, Scanzoni,[11] Bollinger, von Recklinghausen, Schmorl, Ribbert, Aschoff and Albrecht[12] deny its existence in the adult. It is as difficult to prove the actual primarity of tuberculosis of the breast as it is of the genital organs. This does not apply to cases of direct inoculation, for well-attested instances of the latter are on record. Thus, Pluyette[1] reports primary tuberculosis of the breast in a girl aged twenty-three years, who was infected through a slight abrasion of the nipple, and Spinelli[13] speaks of a woman who developed the disease after intercourse with a male who suffered from tuberculosis of the testicle.

Whenever the infection is conveyed by means of the circulatory systems the question always arises whether, if autopsy were possible, the primary focus of the disease would not be found in the visceral organs more often affected by tuberculosis. Without an autopsy, therefore, a diagnosis of primary tuberculosis is not scientifically justified.

Primary genital tuberculosis does occur, however, and Veit,[22] after scrutinizing all of the available cases, accepts 15, 10 of the tubes and 5 of the uterus, as actual primary forms.

There are no cases of primary tuberculosis of the breast on record in which the diagnosis was made after autopsy. But as the primary form occurs in the genitalia, it is reasonable to suppose that it may develop in the breast. It is certain that tubercle bacilli may produce characteristic lesions remote from their point of ingress without affecting the parts through which they pass. Dobroklonski,[18] working under Cornil, and Ravenel[18] have produced experimentally primary tuberculosis of the lungs through the alimentary tract without any lesion of the tract itself. Attention has recently been directed to the tonsils as frequent portals of entry for the tubercle bacillus. That tubercle bacilli may be present in the tonsil without producing any anatomical alteration is evident from the work of Friedmann.[18]

Goodale and Hendelsohn[14] have observed that the tonsils possess marked absorptive powers. The crypts of the tonsils represent afferent lymph vessels, and carmine granules placed on the tonsils are rapidly absorbed and pass thence through the interfollicular tissue to the efferent lymphatics. As these facts might explain the occurrence of primary tuberculosis anywhere in the economy, we may accept, for clinical purposes at least, those cases of tuberculosis of the breast as primary in which there is no evidence of tuberculosis elsewhere, even after the most careful physical examination.

The importance of primary tuberculosis of the breast lies in the possibility of its transmission from the mother to the nursing child. While it would be quite unusual, at least in the better classes, for a woman with any disease of the breast to suckle her infant, yet Coles[7] saw, in the out-patient department of the Philadelphia Polyclinic, two women with tuberculous breasts nursing tuberculous infants, and Davis[7] believes that he has made the same observation at the General Hospital in Vienna.

So far as I know there is but one case in which tuberculous infection of the child has been traced to its mother's milk. This case, reported by Roger and Garnier,[10] may be briefly summarized as follows:

A pregnant woman came under observation on February 16th, suffering with pharyngeal tuberculosis. On March 7th she gave birth to a child that weighed 2685 grams. The infant was nursed until March 12th, when, on account of the progressing illness of the mother, it was weaned. On March 24th the woman died, and at the autopsy tuberculosis of the lungs and other viscera was noted. The child gradually failed and died on April 25th from tuberculosis of the mesenteric glands, spleen, and kidneys. Two guinea-pigs were inoculated with the milk of the mother on March 11th. Both of these pigs died, one with tuberculosis, the other with fibrous peritonitis and enlarged lymph glands; no tubercle bacilli nor actual tubercles were found in the second case, but the lesions were evidently due to the tubercle bacillus.

While such an observation is exceptional in woman, it has been frequently made in the cow. Pearson[17] quotes many instances of infection arising directly from the milk of tuberculous cattle. Ernst found tubercle bacilli in the milk of 33 per cent. of cows in which a complete post-mortem showed that while the animals were widely tuberculous the udder was free; and Hirschberger, by the experimental inoculation of milk, produced tuberculosis in 55 per cent. of cases from tuberculous cows whose udders showed no sign of disease.

We may therefore believe that the milk of a tuberculous woman is always dangerous for the child, and that, although rare, tuberculosis of the breast may occur in a primary form and be unsuspected, and that the possibility of this condition ought always to be borne in mind during the period of lactation. If the breast is itself the seat of tuberculosis its milk must be highly infectious, for in the analogous affection of the cow the milk almost invariably contains tubercle bacilli.

There is some difficulty in reaching a satisfactory estimate of the frequency of primary tuberculosis of the breast. Freiburg[6] mentions 50 cases, Scudder[8] 80, Carrel 120. Bartsch[9] has thrown out of consideration all those in which a positive diagnosis was not made. Thus in all of his cases, either there was the histological picture of tuberculosis or the bacilli were found or inoculation experiments were positive. There were but 65 such cases, and this is the number

Bartsch includes in his series. So much for the existence of a tuberculous lesion.

When we attempt to separate the primary from the secondary forms there is difficulty also in determining which are primary. While it is unscientific to diagnose primary tuberculosis of any part without an autopsy, we may safely consider a given lesion primary if there is no evidence of tuberculosis elsewhere. If in a given case symptoms exist which may be attributed to tuberculosis in another part, then the disease of the breast cannot be regarded as primary, although the breast may have been its primary seat. This is the opinion of Piskacek,[16] and with it there are no grounds for disagreement.

Tuberculosis of the breast as a secondary lesion has no especial significance, whereas the fact that the mammary gland alone may be affected by the tubercle bacillus is of practical importance. It is well recognized, of course, that in the later stages other organs may be involved.

Reviewing Bartsch's series, in 35 there seems to have been tuberculosis elsewhere. All cases designated as being of a scrofulous habit and those in which there was coincident but less-marked tuberculous infection have been excluded. I have also excluded those cases where the affection was first noted in the axilla. Many of the tabulated cases are incompletely reported and details for determining the actual primarity of the case are scanty. At any rate, Bartsch has no more than 30 primary cases, and 2 of these are in the male. To these I have been able to add 12; some of the latter were not included by Bartsch in his list because suitable literature was not available. The impression one has in going over the reports of tuberculosis of the breast is that its primary form is extremely rare. Bull[21] in 1894 had had 185 amputations of the breast; all of these were submitted to histological examination, and in but one instance was tuberculosis found, and that was primary. Since that time Bull has not observed another case, although he has no record of the number of his breast amputations.

If we analyze the entire number of accepted cases in the female we find that of 40 patients, the entire number—

28 were married	70 per cent.
19 had borne children	47.5 "
12 were single	30 "
12 had hereditary taint	30 "
6 had history of trauma	15 "
8 suffered from mastitis during lactation	20 "
2 were directly inoculated	5 "

The youngest patient was sixteen, the oldest was fifty-nine years. From these figures it is difficult to draw many conclusions in regard to the predisposing causes of mammary tuberculosis. While most of the cases were found in married women, the age at which the disease occurs would explain this fact, because most women

between the ages of twenty and forty are married. No case up to this time has been observed in the female before the age of puberty, although Demme reports a case in a male child four days old, due to direct inoculation. There seems to be no direct connection between lactation and the disease; but 47.5 per cent. of the women had borne children. Trauma has played an inconsiderable part. Perhaps the relative infrequency of mammary compared to genital tuberculosis is to be explained upon other grounds. Hegar, Martin, and Amann[11] have dwelt upon gonorrhœa as a predisposing factor in genital tuberculosis. Eisendrath[19] has recently made the same observation and believes that the gonococcus often prepares the soil for a later invasion of the tubercle bacillus. He quotes Casper,[20] who found 33 per cent. of 35 cases of tuberculous vesiculitis to have been preceded by gonorrhœa. Casper believes that an attack of gonorrhœa, especially in those predisposed to tuberculosis, acts like a trauma in aiding its development. It is similar to an injury in syphilis which is able to produce the manifestation of the disease at the injured spot.

Pathological Anatomy. Tuberculosis of the breast occurs in either a (1) confluent or a (2) disseminated form.

The confluent form may be an instance of (*a*) mixed infection or of the (*b*) true tuberculous abscess.

The confluent abscess in the presence of mixed infection is the usual variety. It may involve the entire breast; it breaks down, forming fistulæ, and in the later stages produces retraction of the nipple. There are the usual signs of inflammatory processes in this region; the axillary glands may be secondarily involved.

An abscess purely the result of the tubercle bacillus, the so-called "cold abscess," is quite rare. It forms an elastic fluctuating tumor, mostly well circumscribed and sharply bordered. It is but seldom surrounded by infiltration; the skin remains unbroken and there are no fistulæ. The axillary glands are not involved.

In the disseminated form there are small nodes of the tuberculous disease scattered throughout the breast. There is not much general enlargement of the gland; the skin remains unaltered; the disease is slow in course, years passing, perhaps, without cognizance of the patient. This form is so rare that it is denied by some authors.

Diagnosis. Many tumors of the breast and the inflammatory affections have to be distinguished from tuberculosis. The differential points here would be like those of tuberculosis in other parts and need not be repeated. In suspected cases the mammary secretion should be stained for tubercle bacilli, as was successfully done by Bevan,[7] or animal inoculation should be made. From simple pyogenic mastitis tuberculosis may be, as a rule, distinguished by its more chronic course. Carcinoma usually occurs later in life and is accompanied by retraction of the nipple. This does not often result in tuberculosis except after the formation of sinuses.

Reported by	Age and social state.	Hereditary history.	Previous disease.	No. of labors.	Last labor.	Lactation.	Breast affected.	Original seat of disease.	Trauma.	Treatment.	Duration of cure.	Remarks.	Axillary glands involved.	Upon what diagnosis is based.
Pluyette,	23 years; single.	.....	.....	.....	.....	.....	.....	Breast.	.....	.....	.....	Direct inoculation.	.....	Bacilli were found in the nipple.
Salomoni,	21 years; single.	.....	Nodule in breast 2 years.	.....	.....	.....	Right.	Breast.	.....	Amputation of breast.	2 yrs.	.....	Yes.	Bacilli.
Salomoni,	23 years; married.	.....	.....	.....	.....	.....	Left.	Breast.	.....	Amputation of breast.	4 yrs.	.....	Yes.	Bacilli.
Warthin,	40 years; married.	.....	.....	5	11 mos. before.	Breast pained while nursing 3d child, 2 yrs. before last.	Right.	Breast.	.....	Excision of nodes.	1 yr. ?	.....	.....	Bacilli; histological examination.
Warthin,	39 years; single.	Yes.	Blow on breast 5 yrs. bef're	.....	.....	.....	.....	Breast.	Yes.	Amputation of breast.	Not heard from:	.....	Yes.	Histological examination.
Davis,	17 years; married.	.....	.....	.....	Pregnant 7½ mos	.....	Right.	Breast.	.....	Amputation of breast.	1 yr	Allowed to go to term; baby died in 6 mos. of marasmus.	.....	Bacilli.
Davis,	25 years; single.	.....	.....	.....	.....	.....	Left.	Breast.	.....	Amputation of breast.	8 yrs.	.....	.....	Histological examination.
Powers,	40 years; married.	Yes.	Pain in rt. breast ten years before at 2d child.	6	.....	Never nursed with right breast after second child.	Right.	Breast.	.....	Excision of nodules.	3 yrs.	.....	.....	Histological examination.
Powers,	26 years; married.	.....	.....	1	2½ yrs. before.	Had not used left breast for nursing; no reason given.	Left.	Breast.	.....	Amputation of breast.	3 yrs.	Patient subsequently died of phthisis.	Yes.	Histological examination.
Ely,	35 years; married.	.....	.....	.....	.....	.....	.....	Breast.	.....	Amputation of breast.	Not given.	Direct inoculation.	.....	Histological examination and animal inoculation.
Schifone,	32 years; single.	.....	.....	.....	.....	.....	Right.	Breast.	.....	Amputation of breast.	Not given.	.....	.....	Histological examination and animal inoculation.
Anspach,	59 years; married.	.....	.....	3	17 years before.	.....	Right.	Breast.	.....	Amputation of breast.	1 yr.	.....	.....	Histological examination.

PROGNOSIS. As in genital tuberculosis, the disease in itself is favorable. The result depends upon the existence of visceral complications. Bartsch's data relative to the results of treatment in his series is too meagre to draw conclusions. In my own series of 12 cases, 2 were not heard from after operation; 4 are reported cured within a year; 1 died at the end of three years, and in 1 the after-condition of the patient is not noted. The duration of cure in the remaining cases is put down at 8, 4, 3, and 2 years.

TREATMENT. Although simple evacuation and curettage or extirpation of the diseased nodules alone has sufficed in some cases, the gravity of the disease usually demands amputation of the breast and the removal of enlarged axillary glands.

The details of the case I have added to those found in the literature are as follows:

HISTORY. Woman, aged fifty-nine years, the mother of three children; there is no tubercular history; there is no clue whatever to the probable source of infection. Husband and children are all living and well. Parents died of old age. Patient married at the age of twenty-eight; menopause at forty-eight; last child when forty-two years of age. She always used both breasts during lactation and never had pain in them. Never had any pulmonary disease nor any illness that might be construed as being tuberculous in nature. Three years before coming under observation a nodule appeared in the right breast; it increased slowly in size and caused retraction of the nipple. There was no ulceration. Pain occurred in the right arm.

Treatment. The breast was amputated by Dr. J. G. Clark, who saw the woman in consultation with Dr. James Tyson. I wish to thank these gentlemen for the privilege of reporting the case.

Pathological Report, Path. No. 607.

Macroscopic Description. The specimen consists of an amputated breast including a portion of the pectoral muscle, together with axillary fat and lymph glands. The skin surface is intact; the nipple is considerably retracted, and at this area and to the right of it there is an irregular nodule about the size of a walnut. The mass is not well circumscribed, but fuses with the surrounding tissue. Upon section the breast appears atrophic. Beneath the nipple and continuous with it there is an irregular mass made up of fibrous tissue. Here and there are dark spots which appear to be areas of necrosis. The entire glandular portion of the breast is represented by this nodule. Its fibres are continuous with the trabeculæ of the fatty tissue which makes up the bulk of the specimen.

Histological Description. The surface epithelium and that of the ducts appear normal. The glandular elements are quite atrophic and there is a relative increase of connective tissue. The lymph spaces throughout the specimen are crowded with small cells having

round nuclei which occupy most of the cell body. Such collections are directly continuous with areas comprising giant cells surrounded by epithelioid cells and the small round ones above mentioned. The nuclei of the giant cells are at the periphery, and the picture is typical of tuberculosis. A few sections were stained for tubercle bacilli, but none were found. It is unfortunate that no animal inoculations were made, but as the case was clinically one of carcinoma the specimens had been hardened in formalin before the value of such proof was apparent.

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A CASE OF MERALGIA PARÆSTHETICA.

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I wish to add the following case of meralgia paræsthetica to the number of those already reported:

Mrs. G., white, aged forty-three years, primipara, came under observation complaining of disability in the left thigh. Her father is living and well at the age of sixty-eight. Her mother died of heart disease at the age of fifty. She has one brother and one sister, both living. The former enjoys excellent health, the latter suffers from intercostal neuralgia. A maternal aunt died of cancer of the breast, and a paternal uncle of Bright's disease. Apart from measles and chicken-pox the patient enjoyed good health until the birth of her child nineteen years ago. The labor was difficult and the puerperium was complicated by abscess of the breast and a

mild form of mania, which persisted for three weeks. From recovery her health was good until one year ago, at which time her husband's misfortune in business occasioned an attack of neurasthenia which lasted about six weeks. She is a woman of high-strung temperament, plethoric habit, medium stature, and heavy build. There is no history or sign of alcoholism or syphilis. She uses tea and coffee moderately. There has always been a tendency to constipation. At present she is passing through the changes of the climacteric and suffers from occasional flushings, dizziness, and palpitation. Twelve weeks before seeking medical attention and while in the enjoyment of her usual health she dropped a flat-iron on her right foot, injuring it severely. For one week she was unable to walk, but gradually regained her power, the weakness of her right foot, however, compelling her to throw as much weight as possible upon the left leg. This because of her weight caused much fatigue. Eight weeks after her initial injury she began to notice a peculiar, rather ill-defined feeling of tingling and numbness accompanied by a sense of constriction on the outer side of the left thigh. Except on four occasions this sensation was entirely absent during rest, but appeared shortly after she began to walk or stand and increased to positive pain which grew progressively worse until she was obliged to sit down. These symptoms continued to increase for five weeks from their inception, when she came under observation. It was impossible for her to walk without a limp, but she had no abnormal sensations in the limb, other than those in the outer thigh. Apart from tingling, numbness, and pain she complained at times of intense heat, at others of cold, as though a wet cloth were placed upon the skin. Occasionally the outer side of the thigh felt "like a foreign body," as she expressed it. Menstruation or changes in the weather appeared to have no influence on her condition. Three weeks after the onset of her symptoms she suffered from a slight attack of supra-orbital neuralgia which lasted three days and has not re-appeared. Examination disclosed anæsthesia on the outer side of the left thigh extending in a line from the great trochanter to the head of the fibula, from the 3d to the 36th cm. mark. The area was 4 cm. broad above, 14 cm. broad in the middle, and 8 cm. broad below. Within this region pain, temperature, tactile, pressure, and hair sensations were greatly diminished, particularly those of pain and temperature. Sensibility to the faradic current was likewise markedly decreased. The nerve was not anywhere sensitive to pressure, although this point was carefully investigated several times. There were no trophic changes. The right thigh was examined for perversion of sensibility of all forms, but with the exception of a small area of doubtful tactile anæsthesia at the middle of its outer surface no alteration was found. With the idea of relieving the pain and paræsthesia the patient painted a portion of the thigh with iodine. It set up a severe reaction which was the immediate cause of her

seeking medical attention. Under the use of strychnine, massage, and galvanism her symptoms rapidly improved and in three weeks they had completely disappeared.

Meralgia paræsthetica is the name given by Roth to a peculiar syndrome appearing most commonly, though not exclusively, in the distribution of the external cutaneous femoral nerve. Meralgia paræsthetica, like most other descriptive terms, is unsatisfactory, in that it describes too little, and fails to include the objective symptoms that are such an important part of the disease. On this account Sollier has suggested the name neuralgia paræsthetica, but to this also there are objections, and it would seem better, until we obtain a term based upon a distinct pathological conception, to remain content with Roth's original description. The disease, although it had been several times previously observed and reported by Bernhardt, Pieracini, Musser and Sailer, and others, was not described as a definite morbid entity until 1895, when Bernhardt published his paper in the *Neurologisches Centralblatt.* Since then a considerable number of cases have been reported, although the affection would appear to be not common, or, if it is so, it is often unrecognized. Meralgia paræsthetica may be defined in the words of Musser and Sailer as a "disturbance of sensation on the external surface of the thigh, characterized by various forms of paræsthesia, associated with dissociation and more or less diminution of sensation." Another definition would be to call it an alteration of sensation on the outer aspect of the thigh characterized by pain, dissociation, anæsthesia, and paræsthesia.

The symptomatology of the disease is quite constant so far as the kind of symptoms is concerned, but the combinations in which they appear are very various. They manifest themselves objectively and subjectively. In a large number of cases the subjective symptoms consist of tingling and numbness, slight at first, but increasing in severity as the leg is used, sometimes amounting to a severe ache or pain. Other patients complain of heat and others of a sensation of cold, or both of these may be present at different times in the same patient, as occurred in our case, where at one time the heat was so marked that the patient declared she could almost feel it through her dress, and at another the sensation of cold was compared to a moist cloth pressed against the skin. Sometimes there is hyperæsthesia so great that the slightest touch is unbearable. Musser and Sailer mention an instance of this—the case of a distinguished jurist whose thigh was so sensitive that the very touch of his clothing became unendurable and he was several times obliged to stop walking in order to pull his garments away from his skin. In the vast majority of cases the subjective sensations disappear when the patient is sitting or lying, but sometimes they persist as in our case, where on four occasions they continued despite the fact that the patient was resting quietly in bed.

The objective symptoms are those of anæsthesia, which includes all qualities of sensation in different degrees. In our case the diminution of electrosensibility was so considerable that the patient bore with equanimity in the left thigh a faradic current which caused much discomfort in the right. There is marked diminution of sensibility to pain, touch, and pressure. Our patient presented such a degree of thermoanæsthesia that a test-tube of hot water was recognized as being only lukewarm and ice gave merely an indistinct feeling of cold. In many instances, as pointed out by Bernhardt, there is tenderness of the nerve trunk just in front of and below the anterior-superior iliac spine. This was never present in our case, and, though frequent, is not a constant symptom.

Meralgia paræsthetica is usually an affection of the external cutaneous nerve, but it may be found in the anterior crural nerve, as in the cases of Féré and Möller, or in the external popliteal nerve, as in Sollier's case.

The etiology of the disease is obscure. A variety of causes have been mentioned by different observers, but it would seem that some of them at least are merely coincidences. Thus some have mentioned the presence of constipation and a sedentary life as having an etiological significance, but these terms convey nothing that is definite and bring to our minds no satisfactory information. There are, however, three factors that appear to bear a close relation to the production of the disease; these are infections, traumatisms, and intoxications. In several instances the meralgic symptoms were consequent upon some infectious process. Bernhardt, Roth, Musser and Sailer, and others mention typhoid fever, erysipelas, and influenza. In one of Nartowski's cases the attack followed a pneumonic and in one of Claisse's a malarial infection. Syphilis or its legacy, tabes dorsalis and general paresis, has been reported by Bacelli, Venturi, Pitres, and Möbius. In one case of Bernhardt's there was chronic lead poisoning; and eclampsia, rheumatism, and alcoholism are mentioned by other writers. Traumatism bears oftentimes an apparently direct relation in the production of the disease. In our case the symptoms followed directly upon excessive use of the limb, which may be regarded as a species of traumatism. In one case of Bernhardt's and in one of Knauer's a sword striking against the leg produced the symptoms, and in another of Roth's the affection followed rough walking. The pressure of a heavy army belt caused the symptoms in both thighs in a patient of Musser and Sailer. McCarthy reports a similar case of Spiller's in which the cause of the symptoms was inexplicable until a truss was discovered pressing upon the external cutaneous nerve. A neuropathic habit seems to have some influence in the etiology. Our patient suffered previously from mania and neurasthenia, while during the persistence of her meralgia she was attacked by a slight supraorbital neuralgia. Hereditary influence has been traced by Musser and

Sailer, in one of whose cases the trouble appeared in son, father, and grandfather, and in another the same complaint affected father and daughter.

The pathology of the disease is a mooted question, some authors placing it among the neuralgias, others among the neuritides, and still others denying that it should be classed with either of these diseases. Spiller believes many of the cases are allied to the pressure palsies. Musser and Sailer are of the opinion that it is probably a neurosis. In attempting to classify meralgia paræsthetica we are confronted at the outset by two difficulties: first, our ignorance of the pathological conditions present in each case, and, second, our inadequate knowledge of the exact relations neuralgia and neuritis bear to each other. Many years ago Trousseau pointed out that neuralgia is only a symptom and connotes no constant pathological condition. Neuritis likewise is a common name for different morbid changes. We have, for example, the parenchymatous, the interstitial, and the segmental of Gombault. The two affections are not mutually exclusive. In cases of neuralgia all the various processes of neuritis with degeneration and atrophy of nerve fibres have been seen. On the other hand, many cases diagnosed clinically as neuritis are accompanied by neuralgic pain. Spiller and others have demonstrated marked pathological alterations in the Gasserian ganglion and nerve trunks in trigeminal neuralgia, and Thomas has found very similar changes in the ganglia on the posterior nerve roots in the early stage of tabes, which begins with neuralgic pains. The two conditions, neuralgia and neuritis, overlap, as it were, and perhaps we are not always logical in attempting to separate them. In the few instances in which the nerve has been examined in meralgia paræsthetica pathological changes were sometimes present, as in the cases of Nawratski and Sollier; again, they were apparently absent, as in the case of Souques. But, if we admit a priori that disturbance of function is always accompanied by alteration of structure, however slight and temporary, it would seem that, even in those cases that appear normal, some change has occurred that has escaped detection, either because it is more or less fleeting or because our technique is inadequate. Possibly it will be found that in every case of meralgia paræsthetica some structural change has occurred, and when we know the nature of this we will be able properly to classify it as neuralgia, neuritis, or neuroses.

The treatment instituted in our case was the following: one-fiftieth increasing to one-thirtieth of a grain of strychnine sulphate was given three times each day. For fifteen minutes each day the limb was massaged, and following this the whole thigh was wrapped for half an hour in hot Turkish towels. At the end of a week a mild galvanic current supplemented the above treatment. Rest for the limb was insisted upon, and in three weeks the symptoms had completely disappeared. The employment of strychnine

was suggested by Dana's use of it in trigeminal neuralgia. For a week no other treatment was employed in order that the effects of the drug might be observed. From the first the symptoms began to improve, so that strychnine would seem worthy of a trial in these cases. Electricity in the form of the dry faradic brush was first suggested and used by Roth in a number of cases. Musser and Sailer report a case cured by this means, and Sailer has effected cures in two other cases by the same method. In our case we employed a galvanic current, with the anode on the thigh and the cathode on the lumbar spine with apparently good results. When the disease was attributed to rheumatism salicylic acid was given internally, while Devic employed the drug by inunction. That counterirritation is harmful in these cases was shown unmistakably by ours, where the use of iodine caused a painful dermatitis with considerable subcutaneous œdema. Spiller was the first to suggest resection of the nerve in obstinate cases. The operation has been done by Souques and Chipault on the external cutaneous nerve and in Sollier's case on the external popliteal nerve—in each instance with the relief of the meralgic symptoms. In a case recently reported by Neisser and Pollack, Poupart's ligament was divided, with excellent results.

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SURGICAL SCARLATINA.

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Surgical scarlatina, or scarlatina which follows wounds and operations and bears a direct relation to these, has been recognized for the last forty years as a distinct disease. Although from time to time doubts as to the diagnosis of reported cases have been expressed and the suggestion made that the eruptions in question were due to other causes than scarlatinal infection, on the whole, it has been generally admitted that a wound or injury constituted a predisposing cause to scarlatinal infection, and that such infection should be looked upon as a not uncommon complication of operations or injuries. There are about 174 cases of surgical scarlatina reported in detail in the literature and passing mention is made of many more. The first description of scarlatiniform eruptions after operation was made by Civiale in 1858, but he did not connect such eruptions with scarlet fever. He states that "it is quite common to find, especially in persons with calculi, either during the sharp pains caused by the stone or after a surgical operation, papules, petechiæ, or plaques." During the same year Germain Sée reported a case of general eruption resembling that of scarlet fever and coming on after an operation. These two reports are often cited, especially by the French, as the first descriptions of surgical scarlet fever in the literature; but as neither author believed the rash in question to be really scarlatinal, the credit belongs to the English of being the first to attribute these post-operative eruptions to scarlatinal infection, and to trace a causative relation between the operation and the eruption. Sir James Paget, in 1864, in a clinical lecture on scarlet fever after operations, was the first to turn the attention of the medical world to this subject. He gave the details of a case which has since become classical:

A boy was operated on for stone in the bladder. Two days after the operation he had a general scarlatinal eruption, not more intense near the wound than elsewhere; there was no history of infection, no angina, and no desquamation. One month later he had a considerable hemorrhage from the kidney, followed two days after by a second eruption, accompanied by slight angina, and followed by desquamation.

Paget also stated that the previous year during an epidemic of scarlet fever he had observed 6 cases occurring after operations, which cases he considered not accidental, but due to a peculiar susceptibility to the scarlet fever poison consequent upon the operation. The disease, although true scarlet fever, was modified by the

operation, the usual incubation period shortened, the rash irregular, the angina or desquamation or both lacking. Following upon the publication of this lecture, a number of similar cases were reported; thus, Maunder, Graily Hewett, Callender, Martin, and Henry Lee claimed to have seen scarlatina follow various forms of trauma.

Thirteen years after his first lecture Paget collected and published his 10 cases of surgical scarlatina in his *Clinical Lectures*, and in an appendix to these lectures Howard Marsh added 8 cases, while Thomas Smith stated that he had seen 7 cases of scarlet fever following the operation of lithotomy in 43 children. Paget suggested two possible explanations of the part played by the wound; either it forms a port of entry for the scarlatinal poison introduced at the time of operation by direct inoculation from the hands of the surgeon, or else the poison is absorbed before the operation and remains latent until it is enabled to develop in consequence of the lowered resistance of the body caused by the operation. This latter hypothesis seemed to Paget the more probable. He thought that scarlatina following wounds was far from rare, and that the obscure cases of death occurring shortly after operation in children might be explained as due to such a latent infection.

Paget's views received strong confirmation in the eighteen months following the publication of his *Clinical Lectures*, through three reports of epidemics of surgical scarlatina in different hospitals. Goodhart and Paley collected from the records of Evelina Hospital 25 cases of scarlet fever, 18 of which were surgical cases. The infection was traceable in almost all of these; and all the cases as they developed were sent to the fever ward, where none of them subsequently contracted scarlet fever. These authors hold further that any inflammatory process, not necessarily wounds only, favors the development of the scarlatinal poison, which, entering in the usual way, finds the bodily resistance lowered and develops in consequence of the injury, but not directly through it. Stirling described an epidemic of scarlet fever in the Children's Hospital and one in St. George's Hospital, involving 33 cases in all. He believes that there is a real relation between trauma and scarlet fever, but rejects as unproved the explanation given by Paget; the theory that a lowered bodily resistance due to the operation allows the previously absorbed poison to develop is disproved by the fact that surgical scarlatina is as apt to follow an insignificant operation, such as the aspiration of an abscess, as a major operation.

The epidemic of surgical scarlatina described by Howse occurred in a surgical ward in Guy's Hospital and involved only 4 cases. Howse goes farther than the authors just quoted, saying that surgical scarlatina is much more common than is usually supposed, and that the rash usually described as septicæmic is really scarlatinal.

The French writers of this period, between 1864 and 1880, show themselves much more cautious than the English. Verneuil, at the

time when Paget's first lecture was creating so great a stir, wrote on various post-operative rashes caused by pyæmia, including among them the scarlatiniform rash. His pupil, Tremblay, also asserted that the post-operative rashes called by some scarlatinal are really pyæmic, even in those cases where the accompanying symptoms in many ways resemble those of scarlet fever. Terrillon, in 1877, expresses doubt as to the scarlatinal nature of "surgical eruptions." He quotes Braidwood's description of the rash of pyæmia as an "erythematous scarlet rash," appearing on the third to the fifth day after the initial chill, lasting from five to eight days and disappearing in the same order as it appeared. This description would apply to the rashes usually described as scarlatinal. In fact, Terrillon's case of septic erythema reads exactly like most of those reported under the name of surgical scarlatina.

Aulnas, in 1878, classes under the head of septicæmic eruptions those occurring after surgical operations, those occurring in the puerperium, and those occurring in the course of some internal suppurative disease, inasmuch as they are all due to the same pathological agent. Sanné, in Déchambre's *Dictionnaire*, 1879, states that scarlet fever may occur after trauma, but that such a case does not constitute surgical scarlatina. In his opinion, these cases are simple instances of infection anterior to the injury, and the relation between the wound and scarlet fever is merely one of coincidence. Two or three English writers also take the same stand; thus, Ffolliott, Braxton Hicks, and Dobbin all report cases of scarlatiniform rash following injuries, which they attribute to pyæmia. Cheadle, while admitting that patients with open wounds are extremely susceptible to scarlet fever, nevertheless maintains that a scarlatiniform eruption, not contagious, and not followed by the sequelæ of scarlet fever, appears in various traumatic conditions independently of the scarlatinal poison. Litten, in Germany, also describes a septic eruption so like that of scarlet fever that he knows no absolute means of differentiation. Desquamation may follow this eruption and may be quite like that of scarlet fever.

The study of surgical scarlatina received a new impetus in 1881 at the meeting of the International Congress in London. Riedinger, of Würzburg, reported 14 cases of surgical scarlatina which occurred when there was no medical scarlatina in the vicinity. He had no doubt as to the diagnosis in these cases, although the fact that severe inflammatory changes were present in 4 cases might have aroused his suspicions. The fact that the disease was apparently noncontagious in all but 1 case is also mentioned, but not as throwing doubt on the diagnosis. The clinical details are not very satisfactorily given; angina is mentioned in only 4 of the 9 cases; desquamation in 3.

Marsh, in a paper before the same Congress, supported Paget's theory as to surgical scarlatina, and pointed out the fact that the

disease had almost disappeared from the Children's Hospital since the building of an isolation ward for fever cases.

An important thesis written on surgical scarlatina in 1882 by Batut, a pupil of Trélat, has been overlooked by the majority of writers on this subject, and is not quoted even by those who hold similar views. Batut's contention is the same as Sanné's, that there is no relation of cause and effect between traumatism and scarlet fever, but only a simple coincidence. Like Stirling, Batut refuses to believe that a predisposition could be created by so slight an operation as the aspiration of an abscess. In his review of the cases published up to this time, he does not call in question the diagnosis, but only the assumed relation between the trauma and the development of scarlet fever. Batut states that he has followed in this thesis the views of his master, Trélat, who published 3 cases of surgical scarlatina in 1878 and 3 more in 1881, but who afterward came to regard the English theory as unfounded, and the relation between scarlet fever and trauma as accidental, not inherent.

Hoffa's critical review of the literature on this subject is frequently quoted. While accepting the English view he rejects most of the reported cases, admitting only those in which the eruption started at the wound. He makes, therefore, a sharp distinction between scarlet fever as an intercurrent disease and true surgical scarlatina, and he also warns against confusing the latter with the rashes due to vasomotor disturbance or to the absorption of poisons, especially carbolic acid.

Brown also insists upon a careful distinction between a scarlatinal rash proper and a scarlatiniform eruption resulting from sepsis or drug poisoning. He gives 2 instances of carbolic acid rash which are interesting, because in both he based his diagnosis entirely on the absence of sulphates in the urine, a point not mentioned by any other author, although many have described cases which had been freely treated with carbolic acid. (Henoch, Goodhart and Paley, Marsh.) Hoffa stated that desquamation does not follow the rash of carbolic-acid poisoning, but there was desquamation in Brown's cases.

In 1887 Murray published a description of an epidemic of scarlet fever in a surgical ward. There were 27 cases in the ward, 23 surgical and 4 medical. Six of the surgical cases took scarlet fever, as well as 1 of the 4 non-surgical cases. The proportion seems about the same, but Murray thinks that the increased susceptibility of the wounded is proved by the fact that of the 4 non-operated patients none had had scarlet fever previously and only 1 took it, while of the 23 operated patients, 5 had already had it and 1 of those 5 took it. The details given in these cases are very meagre, and the changes in the wounds are not noted; but only 1 case had been treated antiseptically. At the same time there were in the ward 6 other surgical cases which showed slight symptoms of septic infection, as anoma-

lous rashes, or a red area surrounding the wound; but these had all been dressed antiseptically and none had symptoms of any severity. Murray considers that the disease was the same in all—surgical scarlatina; but in the last series the action of the poison was entirely local, owing to the use of antisepsis.

A frequently quoted treatise on this subject is Koch's thesis in 1892. Koch reports 31 cases of surgical scarlatina, which occurred in the Kinderspital in Basel, 15 of them tracheotomy cases. He thinks a tracheotomy wound especially liable to scarlatinal infection, for it cannot be kept entirely aseptic, but is always more or less exposed to the air.

Two articles appeared in 1895 within a few months of each other, in both of which surgical scarlatina, while treated as a real affection, is made to seem only one manifestation of an infectious agent, which may in another patient cause erysipelas, puerperal fever, phlegmon, lymphangitis, or ordinary scarlet fever. Ricochon describes a series of cases which he claims were distinctly related, and in which the same infection took different forms in different persons; lymphangitis, scarlet fever, erysipelas, suppuration. Brunner quotes this series of Ricochon in support of his own theory that the same infectious agent can cause phlegmon, lymphangitis, lymphadenitis, and a scarlatinal eruption—that in fact these may be successive stages of the same process. Erysipelas also is due to the same infective agent. He quotes Lenhartz (*Jahrb. d. Kinderheilk.*, 1888), who states that Professor Heubner contracted facial erysipelas after examining the throat of a child with scarlatinal diphtheria; also Braxton Hicks, who states that scarlet fever may be contracted from women with puerperal fever.[1] Brunner thinks that changes in the wound similar to those seen in the tonsils in scarlet fever constitute proof that infection took place through the wound.

Two American physicians undertook to prove experimentally the possibility of infection with scarlet fever through a wound, although the principal object in both cases was to obtain a serum for therapeutic purposes. Ashmead used an adult Japanese, as the people of that race are apparently immune to scarlet fever. He inoculated this man with the scales from a young German who was in the twenty-fifth day of the disease. During the following two days the Japanese had a slight headache, and there was a mild inflammation of the forearm where the inoculation took place. On the third day a scarlet area appeared around the inoculation wound, with fever, redness of the fauces, and itching. The red area remained visible for several days, then faded, and on the eighth day began to desquamate. Stickler's more extensive experiments were made on ten white children, all of whom were in normal health at the time of

[1] In this connection may be mentioned Solly's statement quoted by Lea, that whenever he saw a surgical case becoming phlegmonous he expected to have scarlet fever or erysipelas break out in the same house.

inoculation; he used for inoculation mucus from the throat of a mild case of scarlet fever mixed with 1:600 of carbolic acid and made the injection into the arm. The results, which were published only after Stickler's death, are given in very condensed form and lack many details, and it is hard to know how much importance to attribute to his experiments. The reaction to the inoculation was singularly prompt and uniform, but the disease was not typical scarlet fever. Control experiments with the mucus of non-scarlatinal angina would be necessary to prove the specific nature of the reaction, for there is a strong probability that it was due to septic infection.

A careful and exhaustive review of this subject was given by de Bovis in the *Semaine médicale* for 1902. De Bovis has collected 150 cases from the literature, and although he is not ready to accept all of these, it is apparent that the scrutiny to which he subjects them is not oversevere. For instance, in cases where there is no description of the symptoms, he accepts the term "typical scarlatina" as sufficient. He thinks that the cases reported in the earlier literature, however meagrely, may be accepted also, because, in the pre-antiseptic days, surgeons must have been so familiar with the appearance of pyæmic eruptions that they could hardly have mistaken one for scarlatina. The great diversity of opinion, however, among the earlier writers does not bear out this view.

The most careful article which I have found in the English literature on this subject is Manning's "Skin Eruptions which Occur in Septicæmia following Scarlet Fever and Diphtheria." Without entering into the question of surgical scarlatina, Manning succeeds in indirectly throwing light on several vexed questions concerning it. His views are based upon a study of almost 6000 cases of scarlet fever and diphtheria treated in the City Hospital of Birmingham. In 2.1 per cent. of these cases a condition supervened which he explains as a toxæmia due to "tissue necrosis in septic surroundings" and identical with that often seen in cases of sloughing wounds, puerperal fever, or in the third week of typhoid fever. In his cases the cause was found in the ulcerative processes in the nose and throat. The attack usually came on during the second week, but might be as early as the fifth day or as late as the thirtieth. The first symptoms were: rise of temperature, restlessness, exacerbation of the throat symptoms, followed after about twenty-four hours by a scarlet or pink eruption, which, in the early stages, was in the form of spots with well-defined margins, disappearing on pressure. It appeared over the joints and prominent bony points, while a papular eruption appeared on the arms and legs. In mild cases the eruption faded and did not recur, but in severe cases it spread rapidly and by the second or third day resembled the rash of scarlet fever very closely. Albumin was often found in the urine. Profuse desquamation followed, accompanied by defervescence, and in the majority of cases succeeded by a second rise of temperature and a second

eruption spreading more rapidly than the first, and with an exacerbation of all symptoms. A second desquamation followed this eruption. Most of these cases were fatal, death occurring sometimes after the second rise of temperature, before the second eruption, sometimes after the second eruption, and due usually to septic pneumonia, diarrhœa, or exhaustion. In the non-fatal cases the eruption usually lasted only five days.

Rashes such as these, Manning says, are usually regarded as belonging to relapsing scarlet fever or scarlatinal infection complicating diphtheria, and when the patient is not under observation from the outstart, so that the early features of the rash can be noted, errors in the diagnosis are hard to avoid; for the fully developed eruption usually resembles that of scarlet fever, and the desquamation adds to the confusion. The important point to notice is the distribution of the rash in its early stages. It would be interesting to know how Manning, in the light of his experience, would explain such cases as the classical one of Paget's with its two eruptions, or Brown's case of circumcision followed by gangrene, or Beaudouin's similar case. Verneuil's case of septic eruption had the eruption first over the joint surface.

The literature on the subject of surgical scarlatina thus briefly reviewed comprises 174 cases, the details of which are given more or less fully. To these may be added 10 cases from the records of the Hospital of the Memorial Institute for Infectious Diseases, in Chicago, between October, 1902, and March, 1903. These cases appeared in the Presbyterian Hospital and were transferred to the Memorial Institute.

The first 2 cases, one an operation for tuberculous epididymitis, the second an operation for tuberculous inguinal glands, developed within six days of each other; and a non-surgical case, a male attendant, also developed scarlet fever during this time. The latter had a typical attack with characteristic rash, angina, palpable cervical, epitrochlear and inguinal glands, and characteristic desquamation. The same was true of the second surgical case. The first surgical case, however, was not typical, and, except for the fact that the attendant was apparently infected from this man, his disease would probably not have been diagnosed as scarlet fever, for a sore throat and slight fever were the only symptoms noted until the illness of his male attendant six days later led to a careful examination, when a faint rash was found in the inguinal region, and he was transferred to the Hospital of the Memorial Institute. Later on there was slight desquamation. The wound suppurated for more than three weeks.

No other cases developed in the Presbyterian Hospital until December 22d, when a boy, aged thirteen years, under treatment for tuberculous hip-joint, without abscess, took scarlet fever in the children's ward after a sojourn of three weeks in the hospital. Rash,

angina, strawberry tongue, swollen glands, albuminuria, and desquamation were all present in this case.

Between March 1st and March 6th, 7 children developed scarlet fever in the children's ward. Six of these were surgical cases between the ages of three and ten years, and the operations were as follows: cleft palate, 2; osteotomy, 1; removal of tuberculous glands from the neck, 1. The other 2 were in plaster-of-Paris dressings for tuberculosis of the spine, and for congenital dislocation of the hip-joint. In all 6 cases there was a rash, swelling of the cervical, inguinal and epitrochlear glands, and desquamation. Angina was absent in both of the cleft-palate cases; albuminuria was absent in all. The osteotomy case was the only one in which there was any interference with union in the wound. Slight suppuration along the line of incision persisted in this case throughout his stay in the hospital.

In December, 1903, a child died of scarlet fever with septic complications. The interne, who had been in constant attendance on the child, assisted at the autopsy, and on the following day noticed pain and redness in the middle finger of the right hand. The next day there was suppuration in the finger, sore throat, general malaise, and a temperature of 102° F. Yellowish patches appeared on the tonsils, which were much swollen. On the third day a faint rash was observed on the upper part of the chest, the neck, and above the scapulæ, and the temperature was 103° F. The finger continued to suppurate for four or five days, and slight scaling appeared on the neck. One week later a scarlet rash appeared on the lower part of the abdomen, which, however, was not followed by scaling. A mild nephritis developed in the course of the third week. Streptococci were isolated from the blood and organs of the boy and from the throat and inflamed finger of the interne. The prosector who performed the autopsy developed a streptococcal sore throat on the day following the autopsy.

These 10 cases might be regarded as surgical scarlatina—certainly they are as typical as many in the literature—or, the first 9 might be diagnosed as scarlet fever occurring in surgical cases, the last as streptococcal infection through an abrasion of the finger. As we have seen, there is ample authority for either of these views.

There are two chief points to be considered in deciding this question: Is the disease reported in the literature as surgical scarlatina really scarlatina? If it is scarlatina, what is the relation between the injury and the disease?

Of course, if we accept the opinion of most earlier writers, and of Fürbringer, Gomprecht, Ricochon, and Brunner among the later, we shall believe scarlatina, whether medical or surgical, to be only one manifestation of the same infection which causes erysipelas and various septic processes. But until it is proved that the streptococcus is the cause and not a complication of scarlet fever, we must continue to believe that the infective agent concerned in scarlet fever,

a disease followed by immunity, is not the same as the infective agent concerned in the large number of septic processes which are never followed by immunity. We are not ready to believe that erysipelas, septicæmia, and scarlet fever are the same disease, however similar their symptoms may be. That the symptoms are similar is undeniable. A cursory comparison of the two classes of cases in the literature, those of "surgical scarlatina" and those of "septic rash," is enough to convince one that the same affection has been given different interpretations by different observers. Scarlet fever, if it is a single disease—Gerhardt hazards the bold hypothesis that it is really a group of diseases—is admittedly irregular and polymorphous in its manifestations. It is hard to find two authorities who agree entirely on the cardinal symptoms which must be present to make up a real case of scarlet fever. The rapid onset of the symptoms; the early appearance of a characteristic rash, first on the chest and neck, then rapidly becoming general; the angina; the swelling of the lymphatic glands; the nephritis, and the desquamation make up the typical picture of scarlet fever.

But we may have scarlatina sine febre, sine exanthemate, or sine angina. Jürgensen cites 2 cases of the first; Leichtenstern, 1. The absence of angina in a case with a well-marked rash is rare, but does occur, and the absence of exanthem has also been observed. As for the swelling of the glands, we have Schamberg's statement that the inguinal glands are swollen in 100 per cent., the axillary in 96 per cent., and the maxillary in 95 per cent.; but, judging by the ordinary literature, one would conclude that swelling of any glands, except the submaxillary and post-cervical, was a great rarity, for it is almost never mentioned. Nephritis is insisted on by some as a cardinal symptom, but by many others regarded as a complication only, an instance of infection by pus organisms, and no more essential to the disease than the suppuration of the cervical glands.

Finally, desquamation, which is a tardy symptom at best, may be scanty or atypical, and, even if it is typical in character, proves very little, because it follows other eruptive diseases also, as erysipelas and erythema scarlatiniforme. Jürgensen would lay greater stress on the immunity conferred by a single attack of scarlet fever than on any other symptom, and would, therefore, reject, unless the evidence were overwhelming, all cases in which there was a history of previous scarlet fever or in which there were relapses. This persistent immunity after a single attack, together with the transmission of the infection to others, he regards as the most positive points of evidence.

Given this variety in the symptomatology of scarlet fever, what are the diseases which, in a wounded person, are most apt to resemble it and be confused with it? I say in a wounded person, because the fact that a wound is present complicates the diagnosis very seriously. Jürgensen speaks with great emphasis of the difficulty of differen-

tiating between scarlet fever and sepsis, even in patients without injury or operation; how much more difficult does the question become when an injury is present, and when the symptoms evidently depend in some way upon it?

The surgeons and the dermatologists have much to say on the subject of eruptions which occur in the course of toxic and septic processes, although, except for the French writers, it is seldom that one finds any one of them suggesting that this might be a way of accounting for some of the cases of surgical scarlatina.

Erysipelas is probably the least likely of all the post-traumatic eruptions to be mistaken for scarlet fever, yet Holmes, early in the history of "surgical scarlatina," asserted that most of the eruptions so described were due either to erysipelas or pyæmia. Triwousse was unable to decide on the character of the eruption in his patient before the transmission of the infection in typical form to another person showed that it was erysipelas; his second case, also diagnosed as erysipelas, reads very much like the surgical scarlatina cases of Hoffa, Stirling, Howse, Gimmel, and Ingerslev.

The general symptoms of erysipelas are those of septic poisoning and may simulate closely those of scarlet fever, for the infection often spreads to the mucous membrane of the pharynx, causing either a dry, shining, red appearance, or œdema with swollen tonsils and membranous patches. One cannot help noticing in this connection how often the red throat without the typical scarlatinal changes is mentioned in the cases of "surgical scarlatina" in the literature. The wound may suppurate and become gangrenous; or, as is not uncommon, it may heal rapidly. Bollici's cases are somewhat suggestive of erysipelas. In his first and second cases there were bullæ and blebs around the wounds, in which there was no suppuration; the eruption began in red patches and there was great itching. In his third case the eruption was vesicular, with large blebs around the wound and over the abdomen. Riedinger diagnosed one of his cases as erysipelas, apparently because of the character of the eruption; but when albuminuria, swollen tonsils and desquamation followed, he decided that it must be scarlet fever. The fact that desquamation often follows erysipelas and that the scales are highly infectious has undoubtedly helped in confusing these two diseases.

The rash occasionally seen in diphtheria, especially in cases of mixed infection with pus organisms, is not very uncommon. The authorities are not agreed as to its frequency; Germain Sée found it in 22 per cent.; Mussy says 12.5 per cent.; Cadet de Gassicourt and Sanné only 3.5 per cent. If the views of these authors were compared as to the frequency of "scarlatina complicating diphtheria," the difference of opinion among them might become clearer. At all events, it is an established fact that an erythematous eruption, accompanied by a rise of temperature, may occur at any stage in

diphtheria, that it is frequently very like the rash of scarlet fever, if not indistinguishable from it, and that it is most apt to occur in cases which show symptoms of septic poisoning (Manning). If we examine closely the often-quoted tracheotomy cases in Koch's thesis, the conviction is forced upon us that the symptoms in many of them point either to septicæmia with diphtheritic inflammation and suppuration in the wound, or to multiple embolic infection with slight changes in the wound, but with symptoms of suppuration in the internal organs. In these cases the tracheotomy wound probably permitted the pus organisms, formerly localized in the throat, to escape into the general circulation.

Even more difficult is the diagnosis between scarlet fever and the rashes which appear in septic and pyæmic conditions or as a result of poisoning by drugs. It is to the French that we owe the most thorough work on scarlatiniform and scarlatinoid eruptions. As long ago as 1876 Féréol reported to the Hospital Society of Paris a case of "erythéme desquamatif scarlatiniforme récidivant," in which the eruption closely resembled that of scarlet fever. The tendency to relapse in Féréol's case was so great that it seems to have overshadowed the other symptoms; and this may be the reason that similar cases which had not as yet any history of relapse were not reported as belonging to the same class. At all events, there were very few instances of this disease recorded for years after Féréol's observations. One is mentioned in Allbutt's *System*, vol. viii. p. 541, in which the present attack was the only one, and no relapse had as yet occurred. The author believes that such cases are usually diagnosed as scarlet fever, which was also true of the one which came under his observation. It was an article by Besnier, in 1890, which first made this particular form of erythema known to the general medical world. Besnier and most of the French writers after him distinguish two forms—namely, the "scarlatinoid" and the "desquamatif scarlatiniforme." The "scarlatinoid" simulates scarlet fever very closely, for it comes on rapidly and has more fever, involvement of the viscera and mucous membranes, and more serious results than the "scarlatiniforme," which is apt to be subacute and to last longer; Féréol's case belongs to this latter class. The English and American dermatologists consider this distinction on the ground of acuteness, pyrexia, and duration quite unnecessary and disadvantageous, and they therefore recognize only one disease, erythema scarlatiniforme.

According to the text-books, this disease is "a non-contagious eruption, which simulates true scarlet fever, but differs from it in having most diverse causes instead of one cause"; "a febrile affection occurring idiopathically or in association with septicæmia, pyæmia, autotoxæmia, or drug or food poisoning, its most distinguishing features being the scarlatina-like eruption, the non-contagiousness, and the tendency to recurrence." The fever is apt to

be less high than in scarlatina, the tongue is furred or dry, red and glazed, the angina is mild, and the eruption is apt to appear early and develop rapidly. Desquamation also appears early, sometimes before the eruption has quite faded, and in some cases a second eruption comes on before the desquamation of the first is complete. (Compare Schäffer's case of "Tetanus with Relapsing Scarlatina," also Manning's statements as to septic rashes in scarlet fever and diphtheria.) It is usually more intense than the desquamation of scarlet fever and more apt to cause the shedding of "gloves" and "socks" from hands and feet, and to involve even the nails and hair. (Compare the case of Riedinger, intense desquamation involving two nails; Stickler's case, the hands desquamating twice.) Relapses are the rule, but there are cases reported in which there was only one attack.

The causes of erythema scarlatiniforme are:

1. Reflex vasomotor disturbances after operations on parts rich in nerve supply. This reminds one of the testimony of the early writers and of Hoffa as to the frequency of eruptions after operations on the genito-urinary tract.

2. Autotoxæmia from absorption of the products of tissue destruction after crushing or lacerating wounds. (Compare the third case of Brown, a lacerated wound of the leg; Braxton Hicks' case, strain to the muscles of the hip; and Cameron's third case, crushing of the hand.)

3. Poisoning from drugs, the most important for our purpose being carbolic acid and mercury, so freely used in the early days of antiseptic surgery. Brown's cases of carbolic acid poisoning and Hoffa's case of mercurial poisoning might by other observers have been considered cases of scarlatinal rash.

4. Septicæmia, pyæmia, general gonorrhœal infection, puerperal septicæmia, diphtheria. The diagnosis is not difficult in the absence of a wound, injury, or suppurative process, for then the slight constitutional symptoms, slight involvement of the throat and absence of "strawberry tongue" would serve to distinguish it from a well-marked case of scarlet fever. But if there is already an injury, especially one with septic infection, the question becomes quite different.

The general symptoms of septicæmia are too well known to need recapitulation; but mention may be made of the frequent occurrence of lymphangitis leading from the wound, swelling and tenderness of the lymph glands, the fact that serious general symptoms may follow insignificant wounds, and that the changes in the wound may be profound or very slight.

Brown's case, often quoted as a striking instance of surgical scarlatina, suggests the picture of rapid septic infection following a slight operation. A medical student was operated on for phimosis. At the time of the operation he was hot and perspiring, but presented

no other unusual symptoms. Thirty hours after the operation his temperature was 104° F., he was comatose, and the body was covered with an abundant scarlet rash. There was no angina. The wound became rapidly gangrenous, and death occurred seventy hours after the operation. Inquiry revealed the fact that he had been paying daily visits to a scarlet fever patient for two weeks before his operation.

Bollici thought the diagnosis of pyæmia in his and Moreschi's cases ruled out because there was no pus in the wounds; but the literature of surgery is full of instances in which, with small wounds secreting perhaps only a little yellowish serum, a general pyæmia occurred from lodgement of emboli in the joints, bones, lungs, kidneys, etc. Such a pyæmia may follow the opening, spontaneous or operative, of an old abscess or empyema, or even a simple aspiration, the pus organisms, which were formerly walled in, now being able to escape into the general circulation through the ruptured tissues. There is a very large number of old abscesses among the cases of "surgical scarlatina" in the literature. Long-continued suppuration preceding or following the operation or both are mentioned in 29 cases; gangrene, diphtheritic inflammation, œdema, blebs, and fetid odor in 20 cases.

In such cases the diagnosis between sepsis and scarlet fever becomes very difficult, and must rest largely upon (*a*) the non-contagiousness, as shown by the absence of any history of exposure to scarlet fever or of transmission of the infection to others, together with (*b*) the tendency to relapse, (*c*) the absence of a typical strawberry tongue, and (*d*) an unusually early and long-continued desquamation.

(*a*) As to the non-contagiousness, if we omit Stickler's 10 experimental cases and the 97 concerned in the hospital epidemics, we shall find that only 15 of the 67 remaining have a clear history of exposure to scarlatinal infection, and only 8 have a history of transmission of the infection, although in many cases there was ample opportunity for such transmission; and among these 8 cases some are open to question, for the history of the infected patient is sometimes strongly suggestive of septic rather than scarlatinal infection. (See May's cases, Brown's third case, Hoffa's second case, Riedinger's fourth case.) In others the apparent transmission may have been only a coincidence, as an epidemic existed at the time. (Lea's second case, Beaudouin's case.)

It is hardly probable that the authors would have omitted to mention such important contributory evidence as a history of exposure to infection, or of transmission by infection, if such evidence had been at hand. In several instances an apparent non-contagiousness is noted; "the patient, although not isolated, did not infect any of the other children; . . . there was at the time no scarlet fever in the vicinity." (Riedinger, Strubell, Perlis, Lea, etc.)

(*b*) Relapses or recurrences are noted in Schaeffer's case, in Konetchke's, and in Paget's. Page's case had had scarlet fever twice before, the last attack being only seven months before this one. Brunner's case, one of Murray's, and one of May's had had previous attacks.

In considering the question of the tendency to recurrence in erythema scarlatiniforme, it must be remembered that there is necessarily always a first attack, and that many of these cases were reported soon after their occurrence, before it was possible to know whether or not there would be repeated attacks; others were hospital cases and passed out of the sight of the physician who observed the first attack. Even if there was but one eruption without any recurrence, we might still insist that the case might possibly be non-scarlatinal; for there are on record instances of erythema in which there was but one attack, and which, by their non-contagious character and excessive desquamation, were shown to belong to this class.

(*c*) A "strawberry tongue" is mentioned in only 17 of the 174 cases; more often, especially in those which are most strongly suggestive of septic infection, the tongue is described as furred or coated.

(*d*) The facts as to the time of appearance and length of duration of the desquamation are harder to obtain. In only 46 cases is the length of time given between the appearance of the eruption and the beginning of desquamation; the duration of the desquamation is given in only 16 cases. In 19 cases desquamation began on the seventh day or earlier; in 11 it was on the fifth day or earlier. Brunner's case, Ingerslev's second, and Koch's fourth and seventh cases began to desquamate as early as the fourth day; only 14, on the other hand, began later than the eighth day. It is not possible to find any positive data as to the time which elapses between the eruption and the desquamation in typical medical scarlatina. De Bovis gives the average as the eighth day or slightly later for medical scarlatina, the eighth day or earlier for surgical, and our figures would bear out this statement. Desquamation lasted seven days or more in all the 16 cases in which the duration is given; in 2 the time was twelve days, in 1 thirteen, in 1 fourteen, in 3 fifteen, in 1 nineteen, in 1 twenty-one, and in 1 forty days. (D'Espine and Marignac.) Lannelongue's patient is an instance of a rapidly developing rash with long-continued desquamation. In Schaeffer's case the second eruption lasted eight days, the desquamation twenty-one.

De Bovis lays stress on the slight precocity of the desquamation in surgical scarlatina, and says that in some cases there is no desquamation at all. According to him, this is one of the five points of difference between surgical and medical scarlet fever; the other four being the large proportion of adults affected, the slight angina or absence of angina, the short period of incubation, and the fact that the

eruption is apt to start in a peripheral part near a wound, and to spread in the manner of a lymphangitis.

As it happens, all these points of divergence from true medical scarlatina are points in the diagnosis of erythema scarlatiniforme. This latter eruption, when caused by toxæmia or septicæmia, may come on a few hours after an operation of any kind, or at any time in a long-continued suppurative disease; hence the unusually short or unusually long "period of incubation," namely, the length of time between the injury and the eruption. Erythema scarlatiniforme does not cause a serious angina; redness and swelling only are the usual changes; hence the "slight angina" of surgical scarlatina.

The eruption may begin in any region, and it will be remarked on looking over the cases in the literature that the eruption was very often atypical in its place of origin, even in those cases where it bore no direct relation to the wound. Frequently, also, it was not general, but confined to certain localities, as is true of erythema scarlatiniforme.

The occurrence of lymphangitis is almost indisputably a point in favor of the diagnosis of septic rash. The large proportion of adults attacked is explained by the fact that injuries and operations of all kinds are more common in later life than in childhood, and, therefore, septic rashes are also more common. Finally, de Bovis' statement that the desquamation of surgical scarlatina is more precocious than that of medical scarlatina, and in many instances lasts longer, is, as we have seen, a strong bit of evidence in favor of erythema scarlatiniforme.

It seems, therefore, justifiable to rule out as unproved all those cases in the literature of surgical scarlet fever in which the presence of toxæmia or septicæmia was highly probable and in which the symptoms deviated more or less from those of typical scarlet fever, but not from those of toxæmia or septicæmia.

There remain, however, after the elimination of these doubtful cases, a large number which seem to have been indubitably cases of true scarlet fever. Are these cases of "surgical scarlet fever," or of "scarlet fever in the wounded?" In other words, is the relation between the wound and the disease one of causation or of coincidence?

When we examine the literature for proof of Paget's widely accepted theory that injuries of all kinds predispose to scarlatinal infection, we find that they are distinctly unsatisfactory. There is a general impression, especially among surgeons, that scarlet fever is more apt to occur in wounded persons than in the unwounded, but it is impossible to find convincing proof of this opinion. It cannot be found in the reports of hospital epidemics, not even when medical and surgical cases were kept in the same wards. Goodhart and Paley give no comparative statistics. Murray's cases are so

imperfectly reported and so strongly suggestive of septicæmia that they may be ignored. Howse's epidemic was in the surgical wards. Stirling tried to establish from hospital statistics evidence of an increased susceptibility on the part of operated cases as against the non-operated, but was unable to do so.

Koch's cases seem at first sight convincing, for the number of tracheotomized children who developed scarlet fever symptoms was much in excess of the non-tracheotomized. But if we exclude those which showed symptoms resembling sepsis, such as suppurative and diphtheritic inflammations of the wound, with foci of suppuration in lungs, kidneys, etc., we shall have reduced the number appreciably; and it may be still further reduced, in view of the fact that an erythematous eruption may occur in the course of diphtheria, even where there are no severe septic complications. In his second series of cases Koch gives no statement as to the number of operated and non-operated cases in the wards.

Much is made of the fact that the epidemics of scarlet fever among the surgical cases in hospital wards gradually ceased after a more complete system of isolation was practised. This must also have been true of the medical cases of scarlatina, and if there has been a gradual diminution in the cases of post-operative rash, it may be explained by the fact that the advance in antiseptic methods and in isolation of septic cases has gone hand-in-hand with the advance in isolation of fever cases. From time to time the question is raised why scarlet fever should be the only infectious disease to enter through a wound, and more rarely the assertion is made that this is not true, that other infectious diseases act in this respect as scarlet fever does, but are overlooked for various reasons. The references to measles in wounded persons are very infrequent, but there are two possible explanations for that. Either, as Goodhart thought, surgical measles is less striking than surgical scarlatina, and simply has not attracted so much attention; or else, which seems more probable, measles is not so apt to be confused with other eruptive diseases as is scarlet fever, and, therefore, the literature of "surgical measles" has not been increased by the addition of cases of septic rash as has certainly been true of the literature of "surgical scarlatina."

Many writers, especially Brunner and de Bovis, consider that there is an additional proof of the scarlatinal infection having entered by the wound when the latter shows inflammatory changes, especially when there is necrosis, diphtheritic inflammation, or gangrene. But this is a proof which can be made to work the other way; for, if there is such a thing as septic scarlatiniform rash, a fact admitted by all, then these would be the very cases in which one would look for such a rash.

There are certain cases which are often quoted as proof that a wound may render susceptible to scarlet fever a person who has

hitherto been apparently immune. Such are v. Leube's[1] famous case and the 3 similar cases of Riedinger, all of them physicians, who had been frequently exposed to scarlet fever infection during childhood and in the course of their practice, but were apparently immune until after they had received an injury. In 3 cases the injury was an autopsy wound; in the fourth a pin-prick from a surgical dressing. The 3 cases reported by Riedinger could not have become infected with scarlet fever at the time of the injury, for the autopsies were not made on scarlet fever patients, nor was the bandaged man a scarlet fever patient; indeed, Riedinger particularly insists on the fact that at that time there was no scarlet fever anywhere in the vicinity. We have already seen that Riedinger's cases are among the most unsatisfactory in the literature from the point of view of surgical scarlet fever, and it is unnecessary to discuss them further in this connection. This is not true, however, of v. Leube's case, which is unanimously accepted as the most if not the only indisputable case in the literature. It would require much boldness to refuse to accept this case, although the same clinical picture might be presented by a case of septic poisoning from an ordinary autopsy wound. It may also be suggested that, supposing the disease to have been surgical scarlatina, the fact that v. Leube's apparent immunity was overcome by a slight injury was not absolutely proved; for instances are on record of unwounded adults succumbing finally to an infectious disease, even when they had been repeatedly exposed before without contracting it. Jürgensen tells of a sick nurse of whom this is true. Unless, therefore, this case of v. Leube's is to be regarded as sufficient in itself to prove the causative relation between wounds and scarlet fever, it must be admitted that the literature on this subject does not as yet present such proof.

Conclusions. There are about 174 cases of surgical scarlatina reported in the literature more or less in detail, and passing mention is made of many more. Operations and wounds of all kinds, as well as inflammatory processes, are supposed to predispose to scarlatinal infection.

Surgical scarlatina is said to differ from medical scarlatina in five ways: 1. The large number of adults attacked. 2. The shorter period of incubation. 3. The mild angina or absence of angina. 4. The fact that the eruption begins at the wound or in some other unusual region. 5. The slightly precocious desquamation.

Proof of the existence of a special form of scarlatina occurring in connection with wounds rests upon the large number of cases recorded in which an eruption resembling that of scarlet fever fol-

[1] V. Leube had been frequently exposed to scarlet fever in childhood and in his practice. During an autopsy on a severe case of scarlet fever he wounded his finger, and the wound became painful. On the seventh day he grew ill with fever, vomiting, and angina. On the eleventh day a scarlet exanthem appeared, first in the form of a broad, red stripe from the finger up the arm, then spreading over the body. Desquamation began on this arm.

lowed some injury, and upon the frequency of epidemics of scarlet fever among surgical cases, in the days before complete isolation of fever cases was practised.

Careful examination of the reported cases confirms the view held by most French writers, that the eruption in question is often due to septic infection and is not scarlatinal; and that the variations of so-called surgical scarlatina from the typical form of scarlet fever are not due to the unusual mode of infection, but to the difference in the infectious agent.

In the cases where the disease was undoubtedly scarlatina, there is no convincing evidence that the relation between the wound and the scarlet fever was anything more than one of coincidence.

The statistics of epidemics of scarlet fever in surgical wards in hospitals lack the necessary comparative statistics as to the same disease in the medical wards.

There is, as yet, no convincing proof in the literature that surgical scarlatina is anything more than scarlet fever in the wounded.

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THE INFLUENCE OF DAYLIGHT IN THE PROGRESS OF MALARIA,

MORE ESPECIALLY IN CONNECTION WITH QUININE TREATMENT.

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Dr. A. F. A. King nearly twenty years after he had hypothetically put forward and supported the theory of transmission of malaria by mosquitoes[1] has brought out a new and very interesting hypothesis concerning the biology of plasmodium malariæ,[2] an hypothesis which, as far as I know, has not hitherto been made a subject of discussion in any medical journal or publication, although in it King tries to inaugurate a revolution in the generally accepted treatment of malaria.

I first came across Dr. King's papers when I recently went through the medical publications in order to find, if possible, any casual com-

munication speaking for or against an hypothesis the possible correctness of which would indicate a treatment of malaria entirely opposite to the one proposed by King. King's arguments have, therefore, particularly interested me, but, as they have not convinced me, the following remarks which I should like to bring forward in connection with this matter take the form of an opposing criticism.

Dr. King thinks that he can explain a number of the clinical and epidemiological peculiarities from the supposition that the sporulation of the *plasmodium malariæ* cannot take place in the dark, but only in light, more especially red light, and he, therefore, proposes to treat malarial patients in the dark or in rooms with violet or purple window hangings; in other words, by a negative phototherapy similar to the Finsen treatment of smallpox.

Before I enter upon a more theoretical argumentation, I will refer to some experimental investigations by Harrington and Leaming[3] upon the effect of light on *amœba proteus*, which King takes as being in favor of the correctness of his hypothesis. The two doctors just referred to sum up that part of their experiments, which is of interest in this connection, in the following points:

1. Amœba streams in the presence of red light.

2. Streaming is retarded, stopped, or reversed by rays from the violet end of the spectrum.

3. Further, the effectiveness of the following kinds of light as inhibitors of protoplasmic flow diminishes in the order named: white, violet, red.

From these experiments King draws the conclusion that red light promotes the vital processes of the amœba, while violet light retards them; and, as *plasmodium malariæ* is a naked amœba, he infers that the same thing applies to the latter. Harrington and Leaming, however, distinctly point out in their essay that the streaming of protoplasm in the amœba is again continued after remaining a few minutes in any quality of light, and the point seems, consequently, to be the sudden change of light. Unfortunately, nothing is said about the intensity of the light employed, but, as far as one can judge, it has been comparatively faint, and the experiments seem mostly to point to the fact that a transitory rigor is produced by the sudden change from a light with less refrangible rays to a light with more refrangible rays, or from less intense light to more intense. Only one isolated experiment speaks in favor of a direct inciting effect of the red rays: a sudden change from darkness to red light brought about the movements referred to in the course of ten seconds; in this experiment it is, however, not excluded that the heating effect of the rays has been of importance. The assumption of this inciting effect of red rays (in contrast to those with shorter waves) is in any case not confirmed by the somewhat similar experiments which Dreyer[4] has carried out at the Finsen laboratory. In these

the blue-violet rays were found, in fact, to have an inciting—and in a powerful concentration a destroying—effect, while the amœbæ in the red light remained in about the same condition as in the dark. According to Verworn[5] and Davenport,[6] *amœba proteus* is not at all photopathic. The latter, however, found that the amœba showed itself negatively phototactic to light of an intensity varying from strong diffuse daylight to direct sunlight.

In accordance with the above, I cannot, in Harrington and Leaming's experiments, find any support for King's supposition that the *plasmodium malariæ* requires red light in order that its sporulation may be brought about.

1. King first opposes the supposition which has hitherto been generally accepted, that the warmth of the sun, as such, influences the frequency of cases of malaria, independent of the fact that a certain degree of warmth is, of course, necessary in order that the infection-carrying mosquitoes can live and preserve their activity; in this connection he refers to statements by various writers, and mentions, among other things, that negroes, whose dark skin in a particularly high degree absorbs the heat rays of sunlight, possess relative immunity from malaria. When, all the same, there exists a correlation between intermittent fever and warm climates or seasons, we must, according to King, look for the cause not in the warmth of the sun, but in the light of the sun, upon which depends the sporulation of the plasmodiæ.

All the conditions upon which the supposition was previously based, that warmth is an important factor in calling forth intermittent fever, may, with the same right, be held to be in favor of the view that sunlight plays a part as an etiological factor. When King, however, points out that the inhabitants of the island of Tahiti, according to Quatrefages, are free from swamp fever, although the island is only 18 degrees removed from the equator, and holds that this fact speaks against the theory of warmth being of importance, the same example may just as well be taken as a proof that neither can sunlight be the decisive factor. A more likely supposition, it seems to me, is that the conditions and nature of the soil are unfavorable for the development of anopheles, in the same way as they, in Denmark, for instance, have gradually become so by the reclaiming of swampy land by drainage, etc.

2. Febrile paroxysms appear, as a rule, in the daytime, and only in exceptional cases during the night. Even if febrile attacks at night occur somewhat more frequently than King supposes, it can hardly be denied that they occur with predominant frequency in the daytime, and this circumstance really does seem to speak in favor of daylight in some way or other being able to influence *plasmodium malariæ;* but as long as we have no accurate knowledge of the duration of the sporulation process of the plasmodiæ, the above fact does not tell us anything definite as to whether this effect of light is favorable or the opposite.

3. The fact that negroes are less frequently attacked by malaria than human beings of the white race, King attributes to the dark color of their skin, which hinders the light from exercising its sporulation-inciting influence upon the plasmodiæ in the blood. Even if it is not out of the question that the relative immunity of the negroes may be due to entirely different causes, it must be admitted that King has a good argument in favor of the correctness of his hypothesis; there is, however, every reason to accentuate, as Chappel[7] does, that the clothing of civilized nations as a protection against daylight may, in many cases, to some extent, be taken as an equivalent to the dark but often uncovered skin of the negroes.

4. King next quotes a number of writers, according to whom the frequency of cases of illness in malarial districts decreases during periods of much rain or mist, and he connects this decrease with the lesser intensity of daylight at such periods. I must confess it seems to me more natural to explain this by the supposition that rain and mist diminish the chances of being infected by the stings of anopheles.

5. King, after having drawn attention to various examples of spontaneous cure of malaria, and suggested that the patients in question had perhaps been treated in especially dark hospital rooms, puts forward the following hypothesis: The red blood corpuscles in which the plasmodiæ live gradually increase in size so that some of them are at length retained in the capillaries of the skin, where sporulation is then brought about under the influence of daylight. The fever paroxysm which accompanies this process is followed by the sweating stage, during which the bloodvessels of the skin are dilated, whereby the blood corpuscles therein retained are released and the new generation of plasmodiæ is distributed to the other organs of the body.

King looks for the potent principle of those medicines which have been successfully used against malaria in their ability to alter the optical peculiarities of the blood; some of them (Prussian blue, methylene blue) so color the blood that the rays of red light are kept away from the plasmodiæ, while others (quinine, esculin, fraxin) have the peculiarity in common of being fluorescent, and thereby *accentuating* the violet rays of the spectrum in the blood! According to some investigations, now more than thirty years old, by Jones,[8] Rhoads and Pepper,[9] the blood and most of the tissues in human beings and animals are slightly fluorescent; in malarial patients this fluorescence is considerably reduced, while it again increases by the taking of quinine. King sees in this proof that the healing effect of quinine upon malaria is due to its fluorescence; he seems, however, to attach more importance to the beneficial effect of red rays upon the plasmodiæ than to the detrimental effect of violet rays, and he recommends the following treatment of malaria: "Keep malarial patients in dark rooms or in rooms with

violet or purple windows; clothe them with garments impenetrable to light. Give the patients such remedies as render the blood dark or violet or lessen its translucency."

After this condensed summary of King's theories and argumentation, I will now proceed to mention some experimental investigations by other writers and some views which, as they will indicate an entirely opposite therapy, may possibly be of interest in this connection.

As is well known, Tappeiner[10] and his pupils have, in the course of the last five years, undertaken a series of most important investigations upon the poisonous effect of various fluorescent fluids in light and in darkness, respectively. It transpires from these investigations that the destroying effect of the substances in question, for instance, upon infusoriæ, is enormously increased by the effect of light. Even if the fluorescent fluids are so much diluted that in the dark they have no apparent detrimental effect upon infusoriæ, the latter, all the same, will be speedily destroyed in such solutions if they are placed in the sunlight or simply in diffuse daylight, which under normal conditions would not lower their vitality. It has been shown that the most effective rays in this respect are those which produce the strongest fluorescence in the fluids in question. I shall not here enter upon the exceedingly interesting question of rendering micro-organisms and animal tissue sensitized to light;* but only point out that the discovery of these phenomena happened during some experiments with the toxicity of various preparations derived from quinine, and that the quinine preparations themselves possess such sensitiveness-arousing qualities.

The surprisingly strong microbicidal effect of which rays otherwise fairly inactive at these and later experiments have proved themselves possessed, with regard to "sensitized" micro-organisms, has led me to look for the cause of the special effect of quinine preparations upon malarial patients in *the power of these preparations to make the plasmodiæ sensitive, so that the latter are destroyed or weakened under the effect of daylight.*

I will now briefly point to some of the circumstances upon which I think I can base this supposition:

1. The special effect of quinine in malaria can hardly be explained as a direct outcome of its toxicity with regard to plasmodiæ, although this undoubtedly is very considerable, and if we look for an explanation of this effect we must not leave out of consideration a peculiarity so distinct as the power to make micro-organisms sensitive in relation to light.

2. Quinine preparations have decided sensitiveness-arousing qualities. Ullmann's[11] investigations show, for instance, that paramæciæ, which are placed in solutions of quinine of 1: 20,000, first die after

* I have dealt comprehensively with this subject in Mitteilungen aus Finsen's medicinske Lysinstitut, 1904, vol. viii. Verlag, Gustav Fischer, Jena.

about five hours when standing in the dark, while they are killed in the course of eight minutes if placed in sunlight, under conditions which generally have no baneful effect upon paramæciæ.

3. According to Jacobson's[12] and Dreyer's[13] experiments, light, even after having passed through a layer of animal tissue, can exercise its microbicidal effect upon the sensitive-made organs. The depth at which it may be possible to obtain an effect will, of course, among other things, depend upon the intensity of the light.

4. The tissues of the human body are pellucid, and even if only a comparatively small portion of the surface of the body is exposed to light, the blood, and with it the plasmodiæ, will, on account of its continuous circulation, all the same be affected by the light.

If the correctness of the views I have here put forward should be confirmed by clinical experiments, *they indicate the advisability of treating malarial patients with sun-baths or electric-light baths, in addition to quinine.*

I have no doubt that Dr. King's reputation, in addition to his interesting and ingenious argumentation, will give an impetus to clinical tests in malarial districts of his hypotheses, tests which it would be a very simple matter to bring about. My object in writing these notes will be attained if they contribute to the possibility being held in view, at such clinical investigations, *that daylight can increase the favorable effect of quinine preparations upon malarial patients.*

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SOME PATHOLOGICAL AND CLINICAL ASPECTS OF ACQUIRED (FALSE) DIVERTICULA OF THE INTESTINE.

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Only a few years ago acquired diverticula of the intestine were looked upon as pathological curiosities, but owing to the work of Klebs, Heschl, Hanau, Good, Hansemann, Fischer, and Graser, more attention has been paid to them, and gradually their importance in relation to other abdominal conditions is becoming known. Even at the present day the direct clinical bearing of this condition is difficult to estimate, as the collected facts are rather meagre.

According to the old classification, diverticula were divided into false and true. The former became identified with acquired, the latter with congenital. The distinction based on the anatomical construction of the walls of these diverticula lay at the bottom of the first classification, but now we know that this, in many instances, is no distinguishing feature. False diverticula were considered mucosal herniæ through the muscularis, their walls consisting of serosa, submucosa, and mucosa. True diverticula, on the other hand, were made up of all the layers of the bowel wall, and Meckel's diverticulum was practically the only representative of this class. Recent work has shown that diverticula similar in structure to the true may develop during the patient's lifetime, and, as they have nothing to do with an embryonic development or a congenital structure, they should not be called true diverticula.

Klebs, Edel, Sudsuki, and others have reported acquired diverticula not due to direct traction on the intestine, in which all the layers of the intestinal wall were represented. In addition, Neumann, Nauwerck, and Hansemann have reported some cases due to direct traction by tumors (myoma, angioma) or by an accessory pancreas. These need not concern us, as they are exceedingly rare. Their production is clearly due to traction, and if they give any clinical picture, it will be due either to the primary disease or to some such pathological change as makes the diverticulum of Meckel give rise to symptoms. Those diverticula of all the layers of the gut wall not due to traction are often called true diverticula, as they differ from the true in no essential detail, as far as their intrinsic structure is concerned. They differ, however, in that they are acquired, and in this respect they and the more common mucosal herniæ above mentioned are grouped together. Both are acquired and both often develop in the same intestine. At times diverticula, with all the layers of the intestinal wall, develop first, and in them

the mucosa is pushed between the muscular bundles and a mucosal hernia results. From all this the distinction, based upon the time in which the diverticula develop, whether congenital or acquired, will surely appear simpler and lead to less confusion.

The acquired diverticula are found in the small intestine, in the appendix, in the colon, sigmoid flexure, and rectum. They are often multiple. At times hundreds have been found in one intestinal tract. It is fairly well agreed that they are most frequently found in the sigmoid, and that, in general, they are much more common than was once thought. Graser found diverticula ten times in twenty-eight cases, and in an investigation carried on by Sudsuki fifteen cases out of forty showed diverticula in the sigmoid. In the small intestine they are rather regular in their position with relation to the circumference of that part of the bowel. Here they develop at the mesenteric attachment, perhaps a little to one side of it, and by their growth gradually separate the leaves of the mesentery. Rarely do they become larger than a walnut—usually they are the size of a large pea or a chestnut; at times microscopic in size (Graser). In the large bowel no such regularity obtains and diverticula are found going into the mesentery or attached to some other part of the circumference of the bowel. Very often they develop in the haustra alongside one of the longitudinal muscular bands, and frequently they grow into the appendices epiploicæ.

As far as their causation is concerned, a unanimity of opinion does not exist. It is generally granted that old people alone show them, and especially such old people as have suffered from long-standing constipation. Klebs finds them in fat people, whereas Hansemann almost emphasizes the leanness of his subject. The former thought they were due to traction exercised on the bowel by the mesentery, whereas Hansemann favors the theory of pulsion from within the bowel. It is evident that Klebs' view would not explain those cases that had diverticula on the side opposite the attached mesentery—traction on the mesenteric side could hardly lead to the development of diverticula on the opposed side. Klebs pointed out that the diverticula on the mesenteric side were in close relation to the vessels of the bowel, and this has been verified by Hansemann and Fischer. On this point there is no doubt.

Heschl, Hanau, and Good, to find the cause of these diverticula, experimented by filling the intestines of human corpses with water and noting where the injected bowels ruptured. They were pleased to find that the rupture occurred regularly into the mesentery, and from this they concluded that here was the weakest part of the bowel; consequently just here diverticula developed. Hansemann went a step farther, verifying what had been "proven"—*i. e.*, the existence at the mesentery of a locus minoris resistentiæ, and, in addition, producing artificially false diverticula in the intestines of older people. These diverticula, he reports, ran along the sheaths

of the veins of the intestine and were similar, anatomically, to those produced by nature during the life of the patients.

Even if we could accept all this work as directly applicable to living conditions, we would still have to explain those diverticula that do not grow into the mesentery. *Why should these be produced by other agents than those leading to the mesenteric diverticula? Why should not all old people have diverticula, provided their bowels have been constipated, for surely they all have similar venous supply?* These investigators have not explained the origin of these structures, and only the anatomical part of their work is reliable.

A priori, one might have supposed that intestines subjected to increasing internal pressure would rupture at the mesentery. Here the bloodvessels normally enter and the many holes or spaces between the muscle bundles are filled during life with tense vessels containing blood. In the dead intestine altogether different conditions obtain. These spaces are all empty and non-resistant to internal pressure, the whole mesenteric wall of the gut being more in the nature of a sieve than of normal intestinal wall. Moreover, the distention caused by the injection of a stream of water resembles but very little the distention of the bowel within the body. In a recent article by Philipowicz the difference between the distensibility of the normal and dead bowel is emphasized. He never succeeded in distending the bowel to nearly the size it had while distended in the body from volvulus. The bowel ruptured long before an equal distention was attained. Chlumsky's experiments on the intestines of dogs throw some light on this side of the question. When he injected small intestines that were still alive, not removed from the normal animal, the rupture occurred opposite the mesentery, whereas, as soon as he worked with intestines removed from the animal and dead some ten or more hours, they ruptured into the mesentery (Experiment 7). In his earlier experiments with conditions approximating the normal, the ruptures never took place into the mesentery (Experiments 1 to 6).

In our experiments the process is peracute, whereas in the life of the individual it is very slow and chronic. If these facts were not enough to invalidate the experiments that have been published, and which I have been able to verify in greater part, the fact that clinically such intramesenteric ruptures are most exceptional, if they ever occur, shows that this is not the weakest part of the gut during life, as the above investigators declared. Frequently, in cases of ileus, the peritoneum and underlying muscle layers tear and separate, not at the mesentery, but usually more or less opposite to its attachment.

Chlumsky has demonstrated the same in the thicker intestines of dogs. First the serosa tears, then the muscularis, and, interesting to say, the circular first, later the longitudinal, and last of all the strong submucosa. All this shows that the weakest portion of the

gut wall is rather at some point on the side opposite the mesenteric attachment, rather than where Hanau, Heschl, Good, and others have placed it.

In studying this question, I proceeded as other investigators have done, and obtained similar results. The intestine, especially the small, ruptured almost regularly between the leaves of the mesentery, but now and again I obtained a rupture on the side opposite the mesentery. In the large bowel, in general, I had the same results, but here the ruptures were more often on the side where no mesentery was attached than in the small gut. The artificial diverticula reported by Hansemann I could not produce.

From all that has just been said, it will be seen that these experiments are valueless, because they do not show the weakest part of the living intestinal wall. Conclusions based on them, as to the origin of false diverticula, naturally must be invalid. Even if we granted that they were allowable, in trying to explain those diverticula that developed on the non-mesenteric side we would again be at a loss. But without going so far, it must be emphasized that the *supposed weakness at the mesentery does not exist, and, as it does not exist, it has nothing to do with the origin of acquired diverticula.*

In 1898 Graser added to our information on this subject, and tried, not without opposition, to connect chronic congestion of the bowel with the formation of the diverticula. A great deal of doubt has been thrown on this by the fact that congestion is not found in every case of diverticula. When the veins of the bowel are overfilled with blood, they must make more room for themselves and put aside the adjacent muscular fibres. This leads to the production of points of less resistance; in fact, almost reproduces the condition that we find when experimenting on the dead bowel. The enlarged spaces about the veins in which the blood is at a lower pressure, or the similar spaces more or less empty when the congestive condition is relieved temporarily by an increased arterial pressure, gives us a sieve-like condition of the mesenteric wall. Whereas Hansemann limited his application of the relation between veins and diverticula to mesenteric diverticula, Graser sees no necessity for such limitation and finds this relation between diverticula and veins, even in the non-mesenteric diverticula, as they occur in the sigmoid flexure. This view of Graser does not explain the diverticula that are not simple mucosæ hernial, but consist of all the layers of the gut wall; and the recent work of Sudsuki can be considered as a fairly conclusive overthrow of the congestion aspect of the question, though in some cases this may be a secondary factor in the development of diverticula. Not satisfied with disproving the general applicability of this theory, by demonstrating that only six out of his fifteen cases of acquired diverticula showed a condition of congestion and a cause for such a condition, Sudsuki, still clinging, more or less, to the older anatomical findings, propounded another theory. He regards a

diminished resistance of the connective tissue about the veins of the bowel as the predisposing cause of this condition, but he also leaves the etiological factors of the non-mesenteric diverticula more or less in the dark, and does not by this theory give any adequate explanation of the diverticula with muscular layers in their walls (of which he reported six instances), which naturally cannot be due to changes in the connective tissue in the vascular spaces, for the whole wall does give way.

No one can deny, after studying acquired diverticula, that the veins and their sheaths have a definite influence on the development of diverticula on the mesenteric side of the intestine, but from the fact that these diverticula often develop on the non-mesenteric sides, where no large veins pierce the bowel wall, it is more than likely that those on the mesenteric side do no more than direct the path along which the diverticula develop. There must be a cause that underlies both the mesenteric and the non-mesenteric diverticula, both those that are made up of serosa, submucosa, and mucosa, and those with these plus the muscular layers. From the similarity of the anatomical picture, it is highly probable that one and the same cause is present, no matter where the diverticula develop. Simple pulsion, due to collections of gas and feces, is not sufficient. If these alone sufficed, all people so afflicted would have diverticula, which is not the case. There must be some change in the resistant powers of the gut wall. The fact that *diverticula occur in old people, in people whose intestines have been more or less worked out, as evidenced by constipation, points to a muscular deficiency, and in this muscular weakness,* I think, *the cause of the formation of false diverticula must be sought.* This diminished muscular strength will explain the production of diverticula in the mesenteric and non-mesenteric parts of the bowel, for in those patients where the repeated increases in internal pressure overcome the diminished muscular strength of the wall, diverticula must result, diverticula of the whole gut wall or of the mucosa, submucosa, and serosa. According to this view, the latter or common form would develop when the muscular weakness is localized to a small area of muscular tissue, and, as in the mesenteric diverticula, the mucosa would be most affected and pushed along the lines of least resistance. The weak muscle bundles would give and be pushed slightly to either side, as is seen in many early and very small diverticula. The numerous vessels on the mesenteric side, especially the veins, would probably point the further path, and the intimate relation to the veins, which obtains in mesenteric diverticula, would be developed. When larger areas of the wall have lost their muscular strength, naturally all the layers of the wall will be found in the diverticula. Moreover, those diverticula with only longitudinal layers of muscle cells in their walls are equally well explained by this view of the process (Chlumsky). It is very probable that the original view of Klebs is, in part, correct, especially

with reference to the production of the diverticula in the small intestine, and that traction on the gut by the mesentery is a factor in the production of the necessary weakness at this point, where these diverticula so regularly occur in the small intestine. That this traction is a reality can be easily demonstrated by distending loops of intestine *in situ* or by noting the enormous tension of the mesentery in ileus cases. Naturally, in those parts of the intestine where no mesentery exists, this cannot be a factor.

The advantage of looking at this process in this way is manifold. It explains the production of all diverticula, no matter whether they are mesenteric or non-mesenteric in position, and no matter what their structure. It does not depreciate the changes that must develop in the muscular strength of an intestinal wall that has been overworked for a long time in emptying a bowel which is more or less in the position of a chronic ileus, due, perhaps, to torpidity of the rectum, without the ability to re-establish an equilibrium by adequate hypertrophy, not to mention the influence of old age. Moreover, it is in perfect consonance with experimental work and clinical observation.

So much for the causation of acquired intestinal diverticula. Before describing those changes in the diverticula which lead to serious consequences and give a more or less definite clinical picture, two facts must be emphasized. Diverticula in the large intestine, especially in the sigmoid flexure and rectum, are peculiar in that they alone are likely to undergo extensive pathological changes. Why diverticula in the small intestine are comparatively harmless cannot be definitely stated at the present moment. Judging, however, from the fact that in the large intestine hardened fecal masses which are lodged in the diverticula probably lead to the further changes, it can be said that the fluid consistency of the contents of the small intestine will probably account for the relative immunity of that part of the bowel from secondary pathological changes. In addition to this constant immunity of the small intestine, it must be emphasized that it is rather the exception than the rule for diverticula of the sigmoid and rectum to give rise to any symptoms. This probably explains the fact that these diverticula have received so little attention from clinicians. In the literature of this subject there are at least eighteen instances of inflammatory processes arising in these diverticula and leading to grave, often fatal, results.

If the mucous membrane of one of these diverticula in the sigmoid be examined, one can readily see an atrophic condition, in which both the epithelium and their glands are altered. Even before ulceration takes place there is visible an infiltration of round cells in the submucosa. As these diverticula are very often filled with hard fecal masses, ulceration of the mucosa, due perhaps to pressure, is liable to result. Such ulceration may lead to changes, both in the adjacent wall of the intestine, to similar inflammatory changes in the

mesentery of the sigmoid, also to similar changes about the bowel. Moreover, should such an ulceration develop rapidly, a perforation into the free peritoneal cavity results. If, however, such an ulceration should lead to the formation of adhesions between the sigmoid and another hollow organ, the perforation will lead to an anastomosis between the intestine and adherent viscus. At times such a diverticulum ulcerates into the mesentery and an abscess is formed between its leaves. At other times such an abscess may form in the wall of the gut or about it, and this may perforate into a hollow viscus, thus establishing a connection between intestine and bladder, this being the organ usually involved by a fistulous tract.

When the inflammatory process about the diverticula in the wall of the intestine has led to marked connective-tissue growth, this, by its secondary cicatricial contraction, occludes the lumen of the bowel more or less completely. Rotter has brought out the fact that these stenoses of the sigmoid and rectum differ, very markedly, from stenoses due to other causes. These are peculiar, in the fact that they are produced not by cicatricial processes in the mucosa and submucosa, but by the chronic inflammatory process in the deeper layers of the gut wall. In addition to this form of stenosis, diverticula lead to stenosis, both as a result of inflammatory changes in the mesentery and perisigmoid adhesions. Both of these are usually combined with the first form described. Perhaps the ileus cases described by Riedel as due to sigmoid mesenteritis are, in some cases, the result of thickening in the mesentery and angular bending of the intestine, caused by primary changes in acquired diverticula.

How often the carcinomata of the sigmoid arise from the chronic ulcerations of one of these diverticula is hard to determine, because so little attention has been paid to these structures. That such a tumor can arise from the mucous membrane of such a diverticulum, a case reported by Hochenegg conclusively proves.

False diverticula in the appendix have been reported by Kelynak, Ribbert, Edel, Fischer, and Mertens. Whether the earlier cases are acquired diverticula is doubtful. In a recent article by Mertens, it has been definitely shown, however, that diverticula are found in this organ, and that, here also, they may prove of very serious consequence. He reports ulceration and perforation of one of these, corresponding with a similar case of perforation of the diverticulum in the sigmoid, which he also reported.

From this short sketch of the pathological conditions that have been found in the eighteen reported cases, it is evident that acquired diverticula are not always as harmless as we are wont to regard them.

As far as the clinical picture is concerned, it, perhaps, would be best to group the reported cases according to the pathological condition found at operation or post-mortem, rather than according to the diagnosis.

1. *Diverticula which Produced Stenosis of the Sigmoid or Upper Rectum.* Of these I have been able to find six instances in the literature. Graser, Fabris, Rotter, Koch, Waldvogel, and Georgi have reported these cases. All were not simple cases of stenosis; for instance, Georgi's case was complicated by an abscess; Waldvogel's by a fistulous tract between the sigmoid and the bladder. Rotter's case shows, in addition to the stenosis, an abscess in the mesentery of the sigmoid, which communicated with the lumen of the intestine through six perforated diverticula. Koch reported a case of Rotter, which also showed perisigmoiditis, with a fistulous tract running to the bladder wall. All these cases suggested the diagnosis of carcinoma of the sigmoid (Rotter's, of the cæcum) leading to intestinal obstruction. The exact condition of affairs was not evident until the involved intestine was examined in detail; then the condition which had seemed, both clinically and at the autopsy, and *in vivo* during the operation, malignant, proved to be nothing but an inflammatory change arising from an acquired diverticulum.

From this it is evident that the prognosis of chronic ileus, due to sigmoid stenosis, even in the presence of a tumor (*e. g.*, Koch's case, where a movable mass was felt in the left iliac fossa; Georgi's case, where a nodular, sharply defined, fixed mass occupied the left iliac fossa; Rotter's case, with a mass as big as a child's head, etc.) must be very guarded. A colostomy above such a stenosis naturally would relieve the patient of the obstructive symptoms, and, perhaps, some of the good results in cases of supposed carcinoma of the sigmoid that have lived for years after the colostomy are just such cases as the above.

2. *Diverticula which Lead to Perforation into the Peritoneum.* In 1870 Loomis reported a case of peritonitis due to infection from a false diverticulum, which, however, showed no sign of rupture. In Georgi's article three other cases are mentioned, two reported by Fiedler in 1868, and one by Hilbert; all three cases had acute perforative peritonitis. Mertens reports a fourth case of peritonitis due to acquired diverticula, which had perforated into the free abdominal cavity. In this case a man, aged forty-five years, who had been constipated on and off, suddenly, after straining, developed a perforative peritonitis. At the operation the origin of the peritonitis was not found, and the patient died.

These cases teach a very important lesson. The sigmoid must be examined in cases of perforative peritonitis when the surgeon is in doubt as to the source of infection.

3. *Diverticula that Lead to Abscesses or Localized Peritonitis in the Left Iliac Fossa.* Georgi's case is an excellent instance of diverticula leading to suppurative processes in the left iliac fossa. Also in his case, which was complicated (as said before under 1) by stenosis, the probable diagnosis of carcinoma was made. This patient died of peritonitis following an exploratory laparotomy, at which the

tumor was declared inoperable. Post-mortem examination showed that the peritonitis owed its origin to the rupture of a suppurative focus about the sigmoid flexure and in its wall. That the tumor, instead of being malignant, was purely inflammatory, due to acquired diverticula. Gussenbauer, according to Mertens, had, many years ago, a similar supposed case of carcinoma of the sigmoid. The local peritonitis, in fact the whole tumor, when the resected gut was examined proved to be inflammatory, due to changes in acquired diverticula.

Such cases make it very clear that we must think of false diverticula when we are brought face to face with inflammatory conditions in the left iliac fossa in elderly people.

4. *Diverticula Leading to Perforation into the Urinary Bladder or Densely Adherent to the Bladder.* These and the stenotic cases are perhaps the most important from a prognostic standpoint. Abnormal communication between the bowel and the bladder suggests usually the gravest of diseases and an inoperable condition. Most of these cases that are due to carcinomata probably never get into the literature, so that a statistical table, such as Chavannaz has published, is of doubtful value. Most surgeons and pathologists, undoubtedly, see such communications most commonly after carcinoma of the bowel. Mikulicz speaks of such as if that were his experience. Still, the fact that in twenty such cases of communication between the bowel and bladder Chavannaz found that nine were inflammatory in origin, five tubercular, four carcinomatous, and two traumatic, is of great interest to us in connection with the question of diverticula. How many of the inflammatory cases were due to perforation of these into the bladder is not known, though the following cases will show that this has repeatedly happened, and that such a possibility must be reckoned with in these bowel-bladder fistulæ.

In the literature I have been able to find several cases of perforation into the bladder due to acquired diverticula. In 1858 Sidney Jones, in the *Transactions of the London Pathological Society*, reports the case of a man who passed feces and gas in his urine, and, finally, died, as the result of difficulty in urinating, because of a fecal concretion in the bladder. At the post-mortem examination a free communication was found between the bladder and a perforated sigmoid diverticulum. According to Waldvogel, Czerny had a somewhat similar case. Waldvogel himself saw a case in which the patient, who had been passing gas in his urine, had a communication between the bowel and bladder by a sinuous fistula. From the fact that the gas was odorless and contained no sulphur, he concluded that it was produced in the bladder. He was able to isolate a gas-producing bacterium, which he thinks wandered in from the intestine by the fistulous tract. In Mertens' article another case attributed to Treves is reported. Koch's case, of which mention has already

been made, under stenosis, showed intimate adhesions to the bladder wall, so that part of this had to be resected. This patient had urinary symptoms, and the natural suspicion before operation was primary carcinoma of the gut, with secondary involvement of the bladder.

Hepner recently reported another case in an old woman. The symptoms came on suddenly after lifting a heavy weight. She had fever and pain in the abdomen and vomiting. Gradually the urine became turbid, and before long she showed all the typical signs of an anastomosis between the bladder and sigmoid. The fistulous tract was tied off by operation, and the condition was clearly shown to be a sigmoid diverticulum which had opened into the bladder.

5. *Diverticula and Mesenteritis.* Most of the cases mentioned have shown more or less marked thickening and contraction of the mesentery. As said before, it still remains to be proven that such changes due to acquired diverticula lead to that form of chronic ileus which Riedel cures by non-operative means. Theoretically, this relation seems plausible, and in a recent article by Brehm this author tries to establish a definite relation between inflammation in diverticula, mesenteritis, and volvulus. In eleven out of twenty cases of volvulus he found well-marked mesenteric changes, but he did not prove the first link in the chain. Perhaps in time that will be made clear.

6. *Diverticula and Appendicitis.* Mertens has given most time to the study of this relation. He found, in 106 appendices taken from corpses, two instances of diverticula, and in twenty-eight diseased appendices removed by operation he found one diverticulum which had perforated during the attack. As the appendix itself is really nothing but a diverticulum and subject so frequently to disease, it is a little doubtful whether false diverticula in this location are of much moment in bringing on the trouble. Prognostically, of course, they are of little or no importance, in comparison with those cases in and about the sigmoid that simulate malignant growths.

7. *Diverticula and Carcinoma.* This relation is shown by just one case, that of Hochenegg (Thirty-first Congress of German Surgeons). The future alone can show how important in the production of carcinomata the chronic ulcerations in false diverticula are.

Whether such cases of intra-abdominal disease as I have just enumerated, due to acquired intestinal diverticula, will be recognized more frequently in years to come, it is difficult to say. Only twenty years ago Virchow spoke of acquired diverticula as an unusual pathological condition, but during these twenty years our views have changed. Perhaps the same will occur in the study of the intra-abdominal conditions due to false diverticula, and before long many cases like the eighteen here gathered will be reported. Then will we be in a better position, I trust, to differentiate between the inflammatory processes due to intestinal diverticula and those malignant diseases for which they are mistaken. Already we

are in a position to profit from the reported cases, both in our treatment and in our prognosis.

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THE COMPLICATIONS OF AMŒBIC AND SPECIFIC DYSENTERY, AS OBSERVED AT AUTOPSY.[1]

AN ANALYSIS OF ONE HUNDRED AND TWENTY CASES.

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In the study of post-mortems on patients dying from dysentery at the General Hospital, I have been impressed with the frequent occurrence of grave complications in this disease, and have paid special attention to the pathological conditions present in the various organs. These conditions have been so constant and so important that it has seemed to me that they should be considered more at length than they are now in most of the text-books upon medicine. In looking up the subject of the complications of dysentery, in the most recent works, including even those of the larger

[1] With permission of the Surgeon-General of the United States Army. Read at the February, 1904, meeting of the San Francisco County Medical Society.

systems, I have been surprised at the relatively scant attention which this subject has received. For instance, in Davidson's excellent article upon dysentery in the second volume of Allbutt's *System of Medicine*, no mention whatever is made of the complications attending the disease. In La Fleur's article upon amœbic dysentery in the same volume, the complications attending it are dismissed in a very few lines, the only ones receiving much attention being abscess of the liver and intestinal perforation. This lack of extensive consideration of the complications of this disease is found in almost all of the more exhaustive works upon medicine. To the author this is surprising, for the reason that in a majority of cases occurring at the General Hospital, death has resulted rather from some complication than from the disease itself. While it is possible, in the class of cases cited, that many of the complications may have been due to campaigning in tropical countries with the incident hardships and lack of hygienic living, yet many of them are so constant that it is impossible not to believe that they are due to the disease, rather than to other factors.

It will be noticed that I have divided dysentery into two forms, amœbic and specific. This division has been made because the clinical and pathological conditions present are so diverse as, in my mind, to clearly separate them. Under the term "amœbic dysentery" is included the dysentery caused by the infection of the intestinal tract with *amœbæ coli*. Under the term "specific dysentery" I include the chronic form of the acute epidemic dysentery due to the bacillus of Shiga. This specific form of dysentery is differentiated from the amœbic form by the absence of amœbæ in the feces, by the occurrence, in a majority of cases, of agglutination of a pure culture of the Shiga bacillus by the blood serum of the patient suffering from the disease, and by the isolation of this bacillus, in pure culture, from the feces or from the intestinal ulcerations.

In a previous communication[1] I have described in detail the pathology of the chronic specific form of dysentery as observed in cases dying from this disease, and have been able, in several cases, to separate from the intestinal ulcerations the Shiga bacillus in pure culture. Although the differentiation of this form of dysentery by means of the agglutination test is not, I believe, entirely reliable, still I may say that in my experience this test has proven of much value. I have made a large number of tests with the Shiga bacillus in cases both of amœbic and specific dysentery, and have been able, in a majority of cases, to separate the two by this method. However, we do not have to depend upon this test in order to distinguish the two varieties, as the finding of the amœbæ in the

[1] The Pathology of Chronic Specific Dysentery of Tropical Origin, American Medicine, October 11, 1902.

feces decides at once whether or no we are dealing with amœbic dysentery.

When, however, the cases come to the autopsy table, the pathology of the two forms of dysentery are so different that there can be no mistake made in deciding with which we have to deal. It is not my intention here to give a description of the pathology of the various forms of dysentery, but simply to say that the pathological conditions present in the intestines in amœbic dysentery are so entirely distinct from those present in the specific form that a glance at the intestine suffices to distinguish them.

In considering the complications of these two forms of dysentery, I have selected for analysis 120 cases, 60 of the amœbic form and 60 of the chronic specific form. I have taken an equal number of cases of both varieties for the sake of comparison. I wish to state that the 60 cases of amœbic dysentery comprise nearly all the deaths we have had from that variety, and it is an interesting fact that the chronic specific form was very much more numerous at this hospital during the early days of the Philippine insurrection than it has ever been since. This agrees very well with the fact that the acute epidemic dysentery (or specific dysentery), as studied by Flexner and Strong, was very prevalent in the Philippines during the early days of the insurrection, but has since nearly disappeared, as I am informed by medical officers who have recently returned from the Islands. That this is true is proven by the fact that almost all of the cases of dysentery now received at the General Hospital are cases of the amœbic variety, whereas during 1899 and 1900 the vast majority of the cases received were of the chronic specific form.

Complications Observed in the Nervous System.

The cerebrum, in nearly every case in which it was examined, showed an increase in the amount of cerebrospinal fluid. This increase was often excessive, the brain being œdematous. Upon section of the brain, the lateral ventricles were invariably found filled with fluid, oftentimes slightly cloudy and the choroid plexus was invariably congested. A peculiar condition noted in all the amœbic cases was the intense congestion of the bloodvessels of the cerebrum. This congestion was very marked in all cases examined, and in about 50 per cent. of the cases minute capillary hemorrhages had occurred, which were scattered irregularly over the surface of the cerebrum; in the cases of chronic specific dysentery, on the other hand, the surface of the brain appeared anæmic, and this was especially true of the cut surface. In 3 cases of amœbic dysentery, and in 2 of the gangrenous stage of the chronic specific form, small areas of softening were noticed in the frontal lobes near the median fissure.

Complications Observed in the Respiratory System.

The most common conditions found complicating dysentery in the lungs were emphysema and bronchopneumonia. Of the 120 cases, 62 showed an emphysematous condition of the lungs, of which 42 occurred in the chronic specific form, the remainder in the amœbic. This condition is probably due, in greater part, to the long-sustained recumbent position of the patient and to the poor circulation which is generally present in these cases.

Bronchopneumonia is the most important lung complication, occurring in 14 cases, 12 of which were of the chronic specific form, and 2 of the amœbic. Perhaps a better name to designate this form of pneumonia is hypostatic, as it is probably due to maintaining the recumbent position for a long period of time, but as the pathological conditions are identical with those found in bronchopneumonia, I have preferred to retain that name. This complication was invariably fatal.

Lobar pneumonia occurred in 9 cases, 7 in the chronic specific form, and 2 in the amœbic. In all the cases it was the cause of death.

Empyema occurred in 11 cases, 10 of them being in the amœbic form of dysentery, and 1 in the chronic specific form. Of the 10 cases occurring in amœbic dysentery, 8 were due to perforation of a liver abscess into the pleural cavity.

A very common condition found at autopsy in both forms of dysentery is a chronic adhesive pleurisy, which occurred in 26 of the cases—19 of the specific and 7 of the amœbic form; in all of these cases the adhesions binding the lungs to the chest walls were very firm and of long duration.

Chronic bronchitis occurred in 16 cases—in 10 of the specific and in 6 of the amœbic form. Acute bronchitis occurred in 2 cases of amœbic dysentery. Acute pleurisy occurred in 8 cases, 6 of them being of the chronic specific form and 2 of the amœbic. Infarct of the lung occurred in 1 case of the chronic specific variety. Pulmonary tuberculosis complicated both forms of dysentery, 10 cases showing this complication; 6 of them of the amœbic variety, and 4 of the chronic specific form. In 6 of the cases death was due to this complication. Abscess of the lung was found in 4 cases; in 2 of the cases the abscesses were very numerous, being metastatic in character, and occurred in the chronic specific form of the disease. In 1 of these cases metastatic abscesses of the kidney were also found. The remaining 2 cases were due to amœbic infection of the lung, in 1 case the abscess being due to the perforation into the lung tissue of an amœbic abscess of the liver, and in the other to primary infection of the lung by amœbæ, a rather rare condition. In nearly every case a chronic venous congestion of the lungs was observed, but I have considered this of sufficient importance to record in but 59 cases. This congestion was, of

course, due to the recumbent position of the patient for a considerable period of time, and in many instances led to the production of a bronchopneumonia. I have only considered the condition as one of bronchopneumonia when the characteristic pathological lesions were present upon microscopic examination of sections of the lung, and I may say here that in all the cases recorded careful microscopic examinations were made of all the viscera, besides the examination of the organs macroscopically.

From a consideration, then, of the complications occurring in the respiratory system in dysentery, it will be seen that the most dangerous are the varieties of pneumonia. It will also be noted that the chronic specific variety of the disease is more often accompanied by serious complications than is the amœbic form. This is especially true of the occurrence of pneumonia, and is, no doubt, due to the fact that in the chronic specific variety the patient is more often compelled to keep to his bed for a longer period of time than when he is suffering from amœbic infection.

Complications Observed in the Circulatory System.

Œdema of the pericardium occurred in 30 cases—in 18 of the chronic specific form, and in 12 of the amœbic form. This condition I have found to be one of the most characteristic complications observed in the fatal cases, and, as a rule, the pericardial cavity was found nearly filled with a clear, straw-colored fluid, although in a few cases small shreds of fibrin were observed. Both layers of the pericardium appeared normal so far as could be judged. Acute pericarditis occurred in 6 cases—in 4 of the chronic specific variety, and in 2 of the amœbic. In both instances found occurring in amœbic infection, the condition was due to the perforation of an amœbic abscess of the liver into the pericardial cavity. In all the cases of pericarditis the effusion was purulent in character and the pericardial cavity was distended by it. Valvular disease of the heart was present in 1 case suffering from the amœbic form of the disease. In this case there was valvular disease of both aortic and mitral valves. Arteriosclerosis was observed in 12 cases —8 suffering from the chronic specific form of dysentery, and 4 from the amœbic form. It is impossible in these cases to say how much alcohol had to do with the sclerosis, although it is reasonable to suppose that in most cases it had some etiological influence. When we take into consideration, however, the fibrosis which occurs in dysentery, especially in the liver, spleen, and kidney, it is impossible not to believe that the arteriosclerosis may be partially due to this general hypertrophy of connective tissue.

An important condition found microscopically in the heart muscle, especially in the chronic specific form of dysentery, is a

brown atrophy of the muscle fibre accompanied by partial fragmentation. This condition, the nature of which is still a disputed point, can be observed in almost every case if careful sections are made from different portions of the heart muscle, and as it occurs so frequently in dysentery, it is, I believe, due to pathological changes in the muscle fibre. This atrophy results naturally in lessened tonicity of the heart muscle, and, therefore, in lessened circulation, thus favoring the chronic venous congestion of the organs, which is so common in both varieties of the disease.

Complications Observed in the Genito-urinary System.

Kidneys. Some pathological condition of the kidneys was observed in almost every case of dysentery which has come to autopsy in this hospital. Thus, of the 120 cases analyzed in this paper, 101 showed some form of nephritis. It must be remembered that I have not diagnosed nephritis in these cases alone from a macroscopic examination of the organs, but also from a careful microscopic examination. There is no complication occurring in dysentery which is so common and, I believe, so important from a practical standpoint as is the occurrence of nephritis. It has been stated by some authorities that nephritis occurs but rarely in dysentery. I cannot understand how such a statement can be made, unless the cases which we receive from the Philippines are exceptional in some way, and this I do not believe. It seems to me that the statement can only be made by those who have had very little experience with the disease. Of the thousands of cases of dysentery which have passed through the General Hospital at San Francisco, I am prepared to state that at least 60 per cent. showed at some time or other evidences of inflammation of the kidney. The urine of at least this proportion showed, at some time or other, albumin and casts, and while the condition in a vast majority of cases seemed to clear up, we must admit that during a certain period of time some form of nephritis was present. This very large percentage is well shown in the fatal cases occurring at the General Hospital, in which 101 presented well-marked macroscopic and microscopic evidences of nephritis in one of its forms. The 101 cases were divided, as regards the type of nephritis, as follows:

Acute parenchymatous nephritis	36
Subacute parenchymatous nephritis	45
Chronic interstitial nephritis	20

As regards the occurrence of these various forms in the two varieties of the disease, they were divided as follows:

Chronic specific form :	Acute parenchymatous nephritis	19
	Subacute parenchymatous nephritis	23
	Chronic interstitial nephritis	6—48
Amœbic form :	Acute parenchymatous nephritis	17
	Subacute parenchymatous nephritis	22
	Chronic interstitial nephritis	14—53

It will be observed that a greater number of cases occurred in the amœbic variety than in the chronic specific. This is an exception to the general rule that complications of other organs, except abscess of the liver, are more frequent in the chronic specific variety of the disease than in the amœbic. This large percentage of cases of dysentery showing marked kidney lesions would seem to indicate that the kidneys are especially susceptible to the poisons which are elaborated during the process of the dysenteric infection. As to the nature of these poisons, we know absolutely nothing; but so far as a careful examination could detect, there was nothing peculiar noticed about the microscopic appearance of the sections of the kidneys, nor could there be detected any accumulation of micro-organisms, nor any evidence of any special form of cellular degeneration. It is interesting to note that chronic interstitial nephritis occurred in 20 cases, because in all these cases the patients were young men in whom such a condition would not be expected. Of course, the question of alcoholism has to be considered in these cases, but I do not believe it had very much to do with the production of the disease, and think rather that the condition was one of overgrowth of connective tissue stimulated by some poisonous material, elaborated during the progress of the disease. The occurrence of so many cases of nephritis complicating the dysenteric process, indicates how important an examination of the urine is, since the non-discovery of this complication will invariably lead to a much less favorable prognosis as regards the course of the dysentery, as treatment will not be directed toward the kidneys.

It is impossible for me to say how many of these cases died from the effects of the nephritis, but I believe a considerable proportion did so, and in many of them the dysenteric lesions were so nearly healed that we were forced to look for the cause of death in some other organ, and I believe the kidney was, in all these cases, the organ at fault. Certainly 101 cases of nephritis occurring in 120 fatal cases of dysentery, which were not selected to show this complication, is very significant, and it seems to me of great practical importance.

Infarct of the kidney was observed in 1 case of amœbic dysentery. Abscess of the kidney was observed in 2 cases; in 1 the abscess being due to a perforation of an amœbic abscess of the liver into the kidney, and in the other it was due to metastatic abscesses, which were found also in the spleen and lungs. Urinary calculi were observed in 1 case of amœbic dysentery. Pyelonephritis was observed in 2 cases; 1 of the amœbic form, and the other of the chronic specific form.

Complications Observed in the Glandular System.

Liver. The most common complication observed in the liver was fatty degeneration, which was present in 42 cases, of which

22 were suffering from chronic specific dysentery and 20 from amœbic. In most of the cases microscopic examination showed the degeneration to be very extensive, whole lobules of the liver tissue being replaced by fat.

The next most frequent complication was chronic venous congestion, which was present in 36 cases, 20 of the chronic specific form and 16 of the amœbic. Microscopically this condition was often found to be very marked, the capillaries being engorged with blood, and in many instances these had ruptured, forming hemorrhagic areas within the organ.

Cirrhosis of the liver was observed in 10 cases, 6 of the chronic specific form and 4 of the amœbic. In all, the condition was one of common interlobular cirrhosis of comparatively slight extent. In those cases which did not present evidence of cirrhosis macroscopically, the microscope revealed what was evidently the earliest stage of the process, as evidenced by a slight increase in the interlobular connective tissue and more or less infiltration of the portal spaces by leukocytes and newly formed connective-tissue cells.

Abscess of the Liver. Undoubtedly the most important complication of dysentery, that is, of the amœbic form, is abscess of the liver. This condition was observed in 24 cases which came to autopsy, of which 22 were suffering from amœbic dysentery and 2 from the chronic specific form. The abscesses occurring in the chronic specific form were metastatic in character, the liver being thickly crowded with minute foci of suppuration.

The frequency of the occurrence of amœbic abscess of the liver in dysentery seems to vary greatly with different observers, as is well shown in the following table. The total number of cases of dysentery observed at autopsy or collected from autopsy records (with the exception of Councilman and La Fleur and Futcher, who give all cases observed) by the different investigators is given, followed by the percentage of those presenting abscess of the liver. All the cases given in the table as observed by myself were amœbic in character, the *amœba coli* being demonstrated in the feces.

Observers.	No. of cases observed.	Percentage.
Kartulis	Over 500	60
Zaucarol	444	59
Edwards and Waterman	699	72.1
Councilman and La Fleur	1429	21
Craig	74	33.7
Futcher	119	22.6
Smith	45	84.4

As will be seen from the above table, the percentage of cases of dysentery showing abscess of the liver at autopsy, as observed by myself, has been very small compared with that observed by others. I can hardly tell how to explain this difference unless most of the cases of amœbic abscess are discovered in the Philippines,

and either end fatally there or are operated upon before reaching this country, whereas the vast majority of cases of dysentery not presenting this complication are returned to this country for convalescence.

As regards the location of the abscesses, it may be stated that they occur most frequently in the right lobe, especially in the posterior and upper portion of that lobe. The following table, showing the location of the abscesses observed in cases coming to autopsy here, illustrates this point very clearly.

Number of case.	Abscesses.			
	Single.	Multiple.	Number.	Location.
1	.....	Yes	6	Right lobe 5, left lobe 1
2	.....	"	8	" " 8, " " 0
3	.....	"	4	" " 3, " " 1
4	.....	"	13	" " 8, " " 5
5	.....	"	8	" " 8, " " 0
6	Yes	.....	1	" " 0, " " 1
7	"	.....	1	" " 1, " " 0
8	.....	Yes	2	" " 2, " " 0
9	Yes	.....	1	Lobus Spigelii.
10	.....	Yes	17	Right lobe 16, left lobe 1
11	.....	"	too numerous to count	In both lobes.
12	.....	"	10	Right lobe 2, left lobe 8
13	Yes	.....	1	" " 1, " " 0
14	.....	Yes	3	" " 3, " " 0
15	.....	"	5	" " 5, " " 0
16	Yes	.....	1	" " 0, " " 1
17	.....	Yes	3	" " 3, " " 0
18	Yes	.....	1	" " 1, " " 0
19	"	.....	1	" " 1, " " 0
20	.....	Yes	very numerous	Right lobe, all but 2.
21	Yes	.....	1	" " 1, left lobe 0
22	.....	.....	30	" " 23, " " 7
23	.....	Yes	4	" " 4, " " 0
24	Yes	.....	1	" " 1, " " 0

In those cases which showed multiple abscess of the liver it was almost invariably found that the oldest abscesses, as shown by their size and the thickness of the abscess wall, occurred in the right lobe posteriorly or near the dome. In only 1 case of multiple abscesses observed did the pathological findings seem to indicate that the abscess formation commenced first in the left lobe. My experience, as given in the above table, is well borne out by the collective investigation made by Roux as to the location of liver abscesses in amœbic dysentery. He collected 639 cases with the following result: 435, or 70.8 per cent., were situated in the right lobe; 85, or 13.3 per cent., in the left lobe; and 2, or 0.3 per cent. in the lobus Spigelii. A study of my cases, as given in the table, will also show that the majority of the cases showed multiple abscess, thus proving that the general opinion that amœbic abscess is nearly always single is a mistake. In fact, some authorities have counted several thousand abscesses in the liver and have separated amœbæ from these abscesses. I have seen instances in which the abscesses were too numerous to count.

Rupture of a liver abscess is of comparatively frequent occurrence, the perforation taking place into the abdominal cavity, the pleura, the pericardium, or into any of the adjacent viscera. In 24 cases observed here, 7 were accompanied by rupture, perforation occurring in the following localities: Right pleural cavity, 5 cases; left pleural cavity and the pericardial cavity, 2 cases. As the location of the rupture of amœbic abscess is of great surgical importance, I have prepared the following table giving the results of various observers as regards this question.

Observers.	Case of liver abscess.	Case of rupture.	Pericardium.	Pleura.	Lung.	Colon.	Stomach.	Bile ducts.	Vena cava.	Kidney.	Lumbar region.
Waring . .	300	68	14	28	15	2	1	1	3	2	2
Dutroulau . .	66	25	2	10	7	1	1	...	...	...	4
Roux . . .	162	54	11	17	14	3	6	2			
Haspel . . .	25	6	4	2							
Cambay . .	10	3	...	2							
Howard . .	6	5	5								
Craig . . .	24	8	and pleura 2	5	...	...	...	...	...	1	

In one case observed at this hospital an amœbic abscess of the liver was operated upon successfully, in which no history of a previous attack of dysentery could be obtained. That an amœbic abscess can occur primarily in the liver without a previous dysentery, has been established beyond a doubt by a case reported by Buxton of a woman dying at the Philadelphia Hospital, in which the autopsy showed four large abscesses in the right lobe and one in the left lobe of the liver, the pus of each containing amœbæ, although the large and small intestines were absolutely normal in appearance. In all probability, the case which I have just mentioned is a similar one to that of Buxton.

It is not my intention here to discuss the etiology of amœbic abscesses further than to say that they are, without doubt, due to the infection of the liver tissue by the *amœba coli*, probably reaching the organ through the portal vein, although Councilman thinks that they reach the liver through the peritoneal cavity after penetrating the intestine. Other authorities regard the lymphatics as responsible for the liver infection.

Bacteriological Examination. In all the cases which came to autopsy, sections were made of the walls of the liver abscesses, and in the majority of cases amœbæ were demonstrated. An examination of the pus from the abscess cavity did not result, as a rule, in a demonstration of amœbæ unless it was removed by scraping from the abscess wall. By the later method amœbæ were demonstrated without difficulty. A bacteriological examination of the pus by means of cultures resulted in about 50 per cent. of the cases showing a mixed infection with some other organism, princi-

pally staphylococci, streptococci, or the *bacillus coli communis.* My observations as regards the bacteriology of the pus in liver abscess confirms that of many other observers who have found that in about one-half the cases there is a mixed infection. It is in these cases, also, that we find the yellow or greenish pus, rather than the reddish or chocolate-colored pus, which is so typical of amœbic infection.

The Spleen. Altogether the most common complication observed in the spleen was cirrhosis of that organ, which was present in 48 cases, 25 of the chronic specific form of dysentery and 23 of the amœbic form. Infarct of the spleen was observed in 7 cases, 5 of the chronic specific form and 2 of the amœbic form. A very common condition found in the spleen was pigmentary degeneration, which was especially noticeable in sections of the organ, the pigment being in the form of irregular collections of fine granules, brownish-yellow in color, scattered especially along the edges of the fibrous trabeculæ and around the Malpighian corpuscles. In 21 cases melanosis of the spleen was very noticeable, 16 of the cases suffering from amœbic dysentery. As, in almost every case the melanosis was due to previous malarial infection, it is of interest as showing how often amœbic dysentery is complicated by malarial fever.

Complications Observed in the Digestive System.

As would be expected, chronic enteritis is the most frequent of all complications in the digestive system. This condition was observed in 70 cases, 42 of the chronic specific form, and 38 of the amœbic. The enteritis present varied considerably, of course, as regards its extent and severity, but it may be stated as a general rule that all cases of dysentery are complicated by an enteritis of at least medium severity, and it is my belief that this enteritis is of very great importance as regards the prognosis as to recovery. Many cases which have died at this hospital have undoubtedly succumbed from the effect of the enteritis, rather than from the dysenteric infection.

Chronic gastritis is next in frequency to enteritis as a complication, occurring in 60 cases, 31 of the chronic specific form and 29 of the amœbic form of dysentery. In all the cases the gastritis present was of severe character, and taken with the enteritis certainly militated greatly against the patients' recovery.

Perforation of the intestine through an ulceration occurred in 4 cases, 3 of them suffering from amœbic dysentery, and 1 from the chronic specific form. All of these cases resulted in death from peritonitis.

Acute peritonitis complicated the dysenteric process in 10 cases, 8 suffering from the amœbic form and 2 from the chronic specific form; 4 of these cases were due to perforation by dysenteric ulcers, and 6 to pus infection from liver abscesses.

In this study of the complications of dysentery, I have tried to call attention to their great frequency and importance, as I believe they are often overlooked, much to the detriment of the patient's welfare. It will be seen that the chronic specific form of the disease is most prolific in complications, and in our experience this form of dysentery has been the most fatal with which we have had to deal. The most serious complications accompanying the disease, either specific or amœbic, are nephritis, abscess of the liver, and chronic enteritis and gastritis. These occurred so frequently, especially the two latter, that treatment should be especially directed toward them.

In conclusion, I append a table showing the complications observed in the 120 cases analyzed, which may prove of service to students of this subject.

Total number of cases 120: amœbic, 60; chronic specific, 60.

Complication.	Total number.		Amœbic dysentery.	Chronic specific dysentery.
Subacute parenchymatous nephritis	45	101	22	33
Acute parenchymatous nephritis	36		17	19
Chronic interstitial nephritis	20		14	6
Chronic enteritis	70		38	42
Chronic gastritis	60		29	31
Venous congestion of lungs	59		24	35
Cirrhosis of spleen	48		23	25
Fatty degeneration of liver	42		20	22
Venous congestion of liver	36		16	20
Chronic pleurisy	26		7	19
Abscess of liver	24		22	2
Melanosis of spleen	21		16	5
Chronic bronchitis	16		6	10
Œdema of pericardium	12		2	10
Empyema	11		10	1
Bronchopneumonia	14		2	12
Cirrhosis of liver	10		4	6
Arteriosclerosis	12		4	8
Pulmonary tuberculosis	10		6	4
Acute peritonitis	10		8	2
Acute pleurisy	8		2	6
Lobar pneumonia	9		2	7
Acute pericarditis	6		2	4
Infarct of spleen	7		2	5
Abscess of lung	4		2	2
Intestinal perforation	4		3	1
Acute bronchitis	2		2	
Pyelonephritis	2		1	1
Abscess of kidney	2		1	1
Biliary calculus	1		...	1
Infarct of lung	1		...	1
Infarct of kidney	1		1	
Urinary calculi	1		1	
Valvular disease of heart	1		1	

REVIEWS.

Clinical Pathology of the Blood. A Treatise on the General Principles and Special Applications of Hæmatology. By James Ewing, A.M., M.D., Professor of Pathology in Cornell University Medical College, New York City. Second edition, revised and enlarged. New York and Philadelphia: Lea Brothers & Co.

Much knowledge and interest have been derived within the last few years from numerous hæmatological studies and from investigations upon the hæmatopoietic organs and histogenesis of blood cells, and to-day the importance which the pathology of the blood bears to scientific medicine in general can scarcely be overestimated. That there should be some ready means of access to the facts concerned in this rapidly developing subject is obvious, and inasmuch as the last two years represent a rapid advance in many divisions of the subject the second edition of Dr. Ewing's book becomes of immediate interest. The enlargement and revisions have succeeded in producing an excellent book. Many valuable additions have been made in the chapter on Technique, where new and useful apparatus is described; but it is rather surprising that no mention is made of Wright's stain, although the Jenner mixture is given. A description of cryoscopy and the serum test for blood form part of the new material in this portion of the text. A very brief account of Ehrlich's theories on immunity is inserted. Rather extensive and valuable additions have been made in the discussions on the morphology of the blood and in the chapter devoted to leukæmia, while in the appendix one finds a paragraph concerning the interesting condition termed by v. Leube "Leukanæmia." In fact, new material has been added in almost all parts of the volume, and in every place one finds mention made of the latest researches on the histology and pathology of the blood.

The bibliography appended to each chapter has been carefully brought up to date, and forms one of the most notable and excellent features of the volume. Some new plates and illustrations have been inserted in the text, but most of them are of the same general character as those in the first edition, and practically all of the old plates are used again. They do not give one a good idea of blood cells, and appear crudely diagrammatic. But, in spite of the illus-

trations, the volume is fundamentally good, and has so many really excellent qualities that as a text-book and treatise for reference it is almost invaluable. W. T. L.

THE FOUR EPOCHS OF WOMAN'S LIFE. By ANNA M. GALBRAITH, M.D. Philadelphia, New York and London: W. B. Saunders & Co., 1903.

WE do not believe that this book fills any need. In a former review the question of the necessity of books of this class was considered, and it does not seem needful to go over the same ground again. Suffice it to say that, while no criticism is called for regarding the statements made in the volume, we are old-fashioned enough to consider the young woman better off without the knowledge here offered.

We are glad to see that hemorrhage of the menopause receives in this edition considerable notice. If the book is to be read by the laity it is well that one of the most important subjects in the whole range of woman's reproductive life be not slighted, as was the case in the first edition of the work. W. R. N.

THE PRACTICE OF MEDICINE. A TEXT-BOOK FOR PRACTITIONERS AND STUDENTS, WITH SPECIAL REFERENCE TO DIAGNOSIS AND TREATMENT. By JAMES TYSON, M.D., Professor of Medicine in the University of Pennsylvania and Physician to the Hospital of the University; Physician to the Pennsylvania Hospital; Fellow of the College of Physicians of Philadelphia; Member of the Association of American Physicians, etc. Third edition, thoroughly revised and in parts rewritten. With 134 illustrations, including colored plates. Philadelphia: P. Blakiston's Son & Co., 1903.

IT is not surprising that a third edition of Dr. Tyson's Practice should be required, for the work is on the whole one of the most thoroughly satisfactory of the more recent treatises on that subject. In the new edition both the text and the illustrations have been somewhat added to, and the revisions are numerous and, for the most part, have been carefully made. A short, clear statement upon paratyphoid fever has been added. In the classification of types of dysentery a change is to be seen whereby "Diphtheritic Dysentery" is replaced by "Bacillary Dysentery."

The difficulties of classification are made evident by the fact that under Infectious Diseases the author has thought it wise to place not only croupous pneumonia, but also bronchopneumonia, chronic interstitial pneumonia, and embolic pneumonias.

In accordance with the prefatory request, we take the liberty of calling attention to a few errors of omission and commission. A curious typographical mistake which has gone through all three editions ascribes the investigation of hypertrophic cirrhosis to "the French clinicians, headed by Charcot and Henoch!" (page 460). Angina Ludovici is classed under Diseases of the Salivary Glands, and the statement is made that it is "an inflammation of the floor of the mouth, beginning in the submaxillary gland" (page 314).

It is somewhat surprising to find no mention either of multiple serositis or of adiposis dolorosa, in view of the considerable attention those affections have recently received.

The value of the book to physicians is much increased by the many references to the literature, while the clear descriptions and systematic arrangement make it admirably fitted for the use of advanced students. L. A. C.

MODERN METHODS IN THE SURGERY OF PARALYSES, WITH SPECIAL REFERENCE TO MUSCLE-GRAFTING, TENDON-TRANSPLANTATION, AND ARTHRODESIS. By A. H. TUBBY, M.S. LOND., F.R.C.S.E., Surgeon to and Lecturer on Clinical and Orthopedic Surgery, and in Charge of the Orthopedic Department at Westminster Hospital; Senior Surgeon to the Evelina Hospital for Sick Children; Surgeon to the National Orthopedic Hospital, etc.; and ROBERT JONES, F.R.C.S.E., Honorary Surgeon to the Royal Southern Hospital, Liverpool; Honorary Surgeon, Liverpool Country Hospital for the Chronic Diseases of Children, etc. London: MacMillan & Co., Limited. New York: The MacMillan Company, 1903.

PROBABLY in no department of orthopedic surgery has more progress been made than in the prevention and treatment of deformities resulting from paralysis, and a convenient, readable monograph setting forth this advance will be certainly very acceptable to the profession. The authors of the book are familiar to the American profession through their numerous contributions to surgical literature. They have not deemed it necessary to do more than mention the older and simpler methods of treating deformities resulting from paralysis, such as tenotomy and mechanical devices, as these are to be found in all standard works on orthopedic surgery. Attention is principally given to the methods of muscle-grafting, tendon-transplantation, and arthrodesis. The book is divided into three sections, the first dealing with Infantile Paralysis or Acute Anterior Poliomyelitis, the second with Infantile Spastic Paralysis, or Cerebral Palsy of Children, and the third with Paralysis and Deformities Arising from Injuries and Diseases of Nerves and Some Degenerations of the Spinal Cord.

Anyone reading this small volume and who has not followed the recent advances made in the treatment of these conditions will be surprised at what present-day surgery is able to accomplish.

The illustrations are not numerous and are usually diagrammatic, but are sufficient to thoroughly elucidate the text.

No physician, and especially those treating children, should fail to acquaint himself with the recent devices for preventing deformity after palsy, and no surgeon should undertake to treat these resulting deformities without a careful consideration of the newer methods described in this monograph. J. H. G.

A MANUAL OF THE PRACTICE OF MEDICINE. PREPARED ESPECIALLY FOR STUDENTS. By A. A. STEVENS, M.D. Philadelphia, New York and London: W. B. Saunders & Co., 1903.

THIS excellent manual is well known to several generations of students within and without the college walls. The many additions and alterations in the text of this (the sixth) edition, rendered necessary by the rapid progress of medicine in these days, are presented with all the author's usual clearness and conciseness of style, which he has acquired by years of practice in guiding the learner's footsteps along the difficult and crowded paths of medicine. Much of the text has been practically rewritten for the present edition, especially the section on diseases of the digestive system. Here the classification has been simplified and such special divisions as "dyspepsia," "peritonitis," and "ascites," very properly suppressed altogether. A little more attention might perhaps have been devoted in this portion to the physical examination of the abdominal organs, especially the stomach and colon. This subject is not formally treated, and we note with some regret that the methods of determining the size of the stomach by inflation have not been considered worthy of mention; the practice of distending the organ with carbon dioxide by administering the two parts of a Seidlitz powder separately is referred to as a routine procedure, it is true; but, as recent developments have shown that it is not always free from danger, some fatalities having been reported after its use, the subject is deserving of some comment. The article on malaria, as was to be expected, appears in a new garb, in keeping with the most recent fashion in etiology and pathology, although the failure to mention microscopic examination of the blood for diagnostic purposes must be characterized as an omission, even in the most compact manual on the practice of medicine. However, the imperious necessity of keeping the volume within certain limits, like charity, would cover many more sins of omission than could be found even by the most carping critic. R. M. G.

CLINICAL EXAMINATION OF THE URINE AND URINARY DIAGNOSIS. A CLINICAL GUIDE FOR THE USE OF PRACTITIONERS AND STUDENTS OF MEDICINE. By J. BERGEN OGDEN, M.D. Second edition, thoroughly revised. Philadelphia, New York and London: W. B. Saunders & Co.

THE special feature of this book, which distinguishes it from others of its type, is the thorough and systematic discussion of the clinical significance of urinary changes. The second portion, which embraces almost one-fourth of the text, is devoted to diagnosis, both of the different forms of kidney disease and of diseases outside of the kidneys, by means of urinalysis. The list of diseases is complete, embracing both general and local disturbances, whether medical or surgical; in short, this part of the work is a complete clinical guide to urinary diagnosis. We do not know any other work that treats this part of the subject so exhaustively. By simply referring to the table of contents the known facts about the urine in any given disease can be ascertained at once and without a tedious search through the entire list of individual normal and abnormal urinary constituents. A short abstract of the clinical symptoms is, of course, added. If the statements in this portion of the book are based on actual observations, either made by the author himself or collected from the literature, they present a vast amount of research and reading, which is, however, fully repaid by the value of the results. One is impressed, after reading the book, by the importance of continuous study of the urine throughout the course of a disease. The second edition has been brought up to date in every respect; even cryoscopy, one of the most recent developments in urinology, finds at least a passing mention. In the classification of diseases of the kidneys the author follows Councilman and the most recent pathologists, whose nomenclature he has adopted, giving the older terms as well, however, for the sake of identification. Thus, "chronic parenchymatous nephritis" has now become "subacute glomerular"; in fact, "parenchymatous" has disappeared altogether from the nomenclature and is replaced either by "diffuse" or by "glomerular." This classification, being based on pathological findings, cannot always be strictly followed in practice, however, as the author himself concedes; but it helps to clarify one's ideas of urinary pathology. That portion of the book which is strictly devoted to laboratory work contains nothing new of any importance; but several of the traditional tests have been discarded. The article on albumin shows careful selection and is particularly well arranged; the directions for detecting albumin include a paragraph on the approximate estimation of albumin in which the author distinguishes eight degrees in the reaction of albuminous urine to the nitric acid test, making it possible to dispense with quantitative estimation in practical work. The book is well illustrated with a

number of colored plates and numerous cuts, and contains much valuable information of a practical sort about the choice and management of apparatus and the best sources from which to obtain them, with many other useful hints. R. M. G.

A Reference Handbook of the Medical Sciences Embracing the Entire Range of Scientific and Practical Medicine and Allied Science by Various Writers. A new edition, completely revised and rewritten. Edited by Albert H. Buck, M.D. Volume VII. Illustrated with chromolithographs and 688 half-tone and wood engravings. New York: William Wood & Co.

In a review of one of the volumes of a work such as this, it is impossible to adequately consider all of the individual contributors. Suffice it to say that no article has come under the reviewer's notice, after a careful search throughout the book, that does not show the most careful work on the part of its author and a most judicious editorial supervision on the part of Dr. Buck. A due sense of proportion prevails throughout, and no subject is dismissed with too slight notice, nor is there undue expatiation upon what might be regarded as unimportant matters.

The present volume contains some contributions which may be singled out as authoritative monographs upon the topics considered in them. We would mention especially the contribution on Teratology by Piersol, probably the best known authority on this subject in the world. In addition to the valuable text, Dr. Piersol contributes a number of most interesting illustrations of monsters, and of the method of their embryological development. The article on Tuberculosis by Councilman is also an especially noteworthy and authoritative exposition of the subject. Dr. M. Allen Starr writes, as might be expected, a most lucid account of the description of the diagnosis of local tumors of the spinal cord. The articles upon the Spleen, by Mall; the Sympathetic Nervous System, by Onuf; and that upon Syphilis, by James Nevins Hyde, are all worthy of the high reputations of their authors.

It speaks well for the editorial ability of Dr. Buck that he should have been able to secure the services of such men as Pilcher to write upon Tracheotomy, and Roswell Park upon Trephining, or, as he apparently prefers to call it, Trepanning. D. Bryson Delavan contributes a most interesting description of the tonsils, and the treatment of their various pathological lesions.

The physician who is fortunate enough to own a set of the Reference Handbook may congratulate himself upon having

acquired a library which may be considered a *multum in parvo* of medical literature. Although the volumes are very bulky they are not unwieldy, and their clear print and handsome appearance places them far above most works of an encyclopædic nature.

F. R. P.

THE DECENNIAL PUBLICATIONS, UNIVERSITY OF CHICAGO. A Description of the Brains and Spinal Cords of Two Brothers Dead of Hereditary Ataxia. Cases XVIII. and XX. of the Series in the Family Described by Dr. Sanger Brown; with a Clinical Introduction by Dr. Sanger Brown. By LEWELLYS F. BARKER, M.D., Professor and Head of the Department of Anatomy. Printed from Volume X. Chicago: University of Chicago Press, 1903.

THE rare and valuable material used as a basis of study for the present monograph is described and worked up with the greatest care and precision. The text is excellently and very elaborately illustrated. Dr. Brown in the clinical introduction gives a résumé of the symptomatology of hereditary ataxia, to which is added a family tree of the cases described by him. A careful clinical report of the two fatal cases follows.

The main portion of the monograph is given up to a study made by Dr. Barker of the topography of the brain and microscopic lesions of the brains and cords of the two brothers. The brains and cords of both cases were relatively small, the cords, medulla, and pons in each case looking smaller in proportion than the cerebrum. The various sulci and gyri showed no deviation from the normal type which could be regarded as standing in relation to the disease from which the family suffered.

The microscopic study revealed degenerations of one system of exogenous fibres of the posterior funiculus (apparently corresponding to the third fetal system of Trepinski), the dorsal nucleus of Clark, the direct cerebellar tract of Flechsig in the lateral funiculus, and its continuation in the restiform body. In addition there was some involvement of the dentate nucleus of the cerebellum and the brachium conjunctivum, and probably also of the inferior olivary nucleus of the medulla oblongata. Corresponding to the degeneration of the white matter of the spinal cord there was an increase in the glia tissue. These lesions correspond almost exactly with what Dr. Adolf Meyer found in another instance from the family which he studied. The degenerations in the posterior funiculus should probably be regarded as systemic. Barker believes that they involve only certain of the stem fibres and collaterals of the intramedullary continnation of the posterior roots, namely, those corresponding to one period of medullation in the embryo.

W. T. L.

MAMMALIAN ANATOMY, WITH SPECIAL REFERENCE TO THE CAT. By ALVIN DAVISON, PH.D. Philadelphia: P. Blakiston's Son & Co., 1903.

THIS little work is an introduction to the study of mammalian anatomy, and as such is sure to prove of great value to teachers and students, especially those working in high schools or educational institutions of a similar nature. Although the book is small in size, it is very thorough and accurate, and the illustrations are particularly worthy of commendation. Each section is followed by a number of "practical questions and suggestions" which will prove very helpful in the classroom. The author writes in a style which is both lucid and concise, and, while popular, cannot be termed unscientific. J. H. G.

A HANDBOOK OF OPHTHALMIC SCIENCE AND PRACTICE. By HENRY E. JULER, F.R.C.S., Ophthalmic Surgeon to St. Mary's Hospital; Consulting Surgeon to the Royal Westminster Ophthalmic Hospital; Consulting Ophthalmic Surgeon to the London Lock Hospitals. With illustrations. Third edition, revised and enlarged. Philadelphia and New York: Lea Brothers & Co., 1904.

THIS work is a satisfactory exposition of modern ophthalmology so far as the subject is capable of presentation in a work of its size. A special feature is the free use of illustrations, both chromolithographs and wood-cuts; while the former are perhaps somewhat overcolored in some cases, the work gains the advantage of being almost an illustrated atlas of the eye.

The seventeen chapters of which it consists, besides appendices, begin with the eyelids and take up in order the diseases of the ocular structures and adnexa; 130 pages, about one-fifth of the whole, are devoted to refraction. Optical fundamentals and the different varieties of the refraction of the eye with a description of the function of accommodation are clearly stated without making special demands upon mathematical knowledge.

It is interesting to compare certain points of practice which are no doubt quite general in England with the corresponding practice in this country. Thus in myopia the author states: "A mydriatic is not as a rule necessary except in young children or when astigmatism is present. After the age of thirty years a mydriatic is seldom necessary." In ordering glasses for hypermetropia the author advises that 1 D. be deducted from the total hypermetropia under the age of twenty years, half a D. between twenty and thirty years and full correction after that age. If the hypermetropia be above

4 D. an additional half or 1 D. must be deducted according to the degree and age. The author endorses the view that myopes of whatever degree should wear glasses constantly as near the full correction as possible. He is somewhat non-committal upon the operation of high myopia and truly says that it is as yet impossible to state definitely whether the progress of the myopia is arrested by the operation.

Presbyopia is corrected by the rule of thumb method which gives so much per year. This method of correcting presbyopia is unfortunately not unknown in this country.

We are pleased to see that heterophoria is given the very subordinate place which it deserves: only five pages. Graduated tenotomies are not mentioned.

The appendix contains 43 formulæ, embracing caustics, collyria, unguents, etc.; 8 interesting plates, semidiagrammatic, by G. S. Keeling, illustrate the normal and pathological histology of the eye. A glossary of Greek derivatives (a few Latin) is an aid to the comprehension of ophthalmological terms. T. B. S.

BIOGRAPHIC CLINICS. Volume II. The Origin of the Ill Health of George Eliot, George Henry Lewes, Wagner, Parkman, Jane Welch Carlyle, Spencer, Whittier, Margaret Fuller Ossoli, and Nietzsche. By GEORGE M. GOULD, M.D. Philadelphia: P. Blakiston's Son & Co., 1904.

IN this volume the author continues the studies of the ill health of distinguished literary people, of which a number were presented in a previous volume. Those whom he now presents are George Eliot, George Henry Lewes, Wagner, Parkman, Jane Welch Carlyle, Spencer, Whittier, Margaret Fuller Ossoli, and Nietzsche. By a careful study of his subjects' life history, as detailed not only in their biographies or autobiographies, but in their works, Dr. Gould has come to the conclusion that in every instance the physical suffering and its induced morbidity, which was apparent in their lives and labors, depended upon eye-strain, which could have been corrected in every case by properly fitted glasses. When one considers the vast variety of symptoms which these various authors presented, it is rather a hard task to bring one's self to believe that every one of them originated from a single common cause. Dr. Gould, however, adduces many circumstances which prove that in most instances, at any rate, there was considerable trouble with the eyesight, and much relief might have been given by proper adjustment of glasses, though it must be confessed that it is rather hard to believe that all their complaints were solely due to eye-strain.

Dr. Gould is certainly a bold man. In his preface he criticises the critics of his previous volume, and candidly states that he thinks the members of the medical profession are not in possession of a true summary of the facts contained in his books because of the "malfunction of their journalists and reviewers." He also charges the neurologists and ophthalmologists with neglecting or treating with contemptuous silence what he considers that he has proved. He reproaches the medical profession in general for neglecting the study of morbid physiology or functional disease in the ardor with which they pursue organic and infectious diseases.

Although we cannot feel that Dr. Gould has proved his point in all the cases which he has stated, nevertheless he makes out a very strong case, and his book will be of value if it can only make the profession realize how much functional disorders of the eyes have to do with the general health.

The work is of interest also from a literary point of view, as a pathological study of certain well-known authors. F. R. P.

ELEMENTS OF SURGICAL DIAGNOSIS. By A. PEARCE GOULD, M.S. LOND., F.R.C.S. ENG., Surgeon to the Middlesex Hospital; Member of the Council of the Royal College of Surgeons of England, and of the Examining Board for England; Member of the Senate of the University of London. Third edition, revised and enlarged. Chicago: W. T. Keener & Co., 1903.

THIS condensed work, presenting the Elements of Surgical Diagnosis, is well known through its previous editions. The present edition shows much revision and much new material, which adds greatly to its value. Although the book is small, there are no illustrations and the print is not large, therefore a vast amount of material is found between its covers. Surgical diagnosis is a subject which needs attention from all practitioners, and it will be found here presented in a very terse and comprehensive manner. Among the changes noted in this edition is a section on intracranial complications of middle-ear disease, which has been added to the chapter on Diseases of the Head. Notable changes are also found in the portions devoted to the abdomen. The present edition will find the same place in the esteem of both the student and the practitioner which its predecessors have won. J. H. G.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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The Cardiac Dulness in Cases of Cancer.—W. GORDON finds that in cases of cancer, particularly where the alimentary canal is involved, there is a remarkable diminution and often a complete obliteration of the area of cardiac dulness when the patient is in the recumbent posture. The possibility of emphysema was always excluded. The writer has observed it in a large number of cases, but gives notes of only 6 to illustrate the sign. He became so convinced of the value of the sign that he risked the diagnosis of cancer on the strength of it, where, otherwise, the evidence was inconclusive, and in 5 consecutive cases the diagnosis proved correct. In non-cancerous cases without emphysema he has failed to find it with three exceptions. It does not occur in sarcoma. Gordon states that all one can claim for it is that when present in a doubtful case it is highly suggestive of the presence of cancer, and when absent at a late point in the case its absence is somewhat suggestive of the absence of cancer.

The writer at first thought that the diminished cardiac dulness was due to diminution in the size of the heart commensurate with the general wasting, but the autopsy findings did not bear this view out. He is inclined to believe that the true explanation is a lessening of the elasticity of the lung tissue, comparable to the loss of elasticity of the skin of the abdomen in cases of visceral carcinoma. This loss of lung elasticity causes a sort of false emphysema, in consequence of which the edges of the lungs gradually close over the front of the heart.—*Proceedings of the Royal Medical and Chirurgical Society, March* 5, 1904.

On the Albuminuria of Puberty.—LOMMEL (*Deutsch. Arch. f. klin. Med.*, Band lxxviii., Heft 5 and 6, p. 541) contributes some interesting observations upon the urine of 587 young employés in the factories of Zeiss and Schott in Jena. The patients were between the fourteenth and eighteenth years. The majority of these patients were under observation from three to four years, the ages being from fourteen to eighteen

years. 111, or 18.9 per cent., showed either once or repeatedly a positive reaction for albumin. In the great majority of cases the albuminuria was intermittent, appearing often at periods far removed from one another. Examinations were made in most cases by acetic acid and ferrocyanide of potassium, part of the earlier examinations having been made by boiling. The amount of albumin was generally very small, and consisted in most cases apparently of serum globulin as well as serum albumin. The amount estimated by Esbach's method was usually from 1.20 to 1.10 per cent., rarely over 1.10 per cent. As a rule, there was no appreciable sediment; sometimes hyaline casts and occasionally fatty epithelial cells were found. Lommel considers the cause of the albuminuria of puberty as in part an evil condition of the blood, in part a slight degree of cardiac insufficiency, with a tendency to passive congestion, diseased circumstances which depend upon puberty in that at the time of the greatest growth of the body and the most active period of development, the new formation of blood does not keep proper pace with the other changes, nor does the heart become fully adapted to the increased demands dependent upon the rapid growth of the body and the correspondingly vigorous development and increase of energy. Lommel was struck by the fact of the very common evidence of cardiac and vascular disturbances among his cases, a part showing the juvenile growth of hypertrophy of the heart described by Sehl and Krehl. Bodily exertion seemed to have little effect on the albuminuria, the early morning urine showing essentially the same features as that of the evening. The early morning examinations were, on the whole, less apt to reveal albumin than those later in the day.

In only two instances he was able to examine into the question as to whether the albuminuria was or was not orthostatic. In each of these instances rest in a horizontal position resulted in the disappearance of albumin, which returned in the erect posture. He was unable to extend his examinations beyond the eighteenth year, but out of 130 patients there were over 25 belonging to just the same class as those examined by Lommel. Professor Matthes found albuminuria in but one instance.

How can the functional albuminuria be distinguished from that dependent upon true organic changes? This Lommel considers extremely difficult, and it can be done only through the possibility of long observation and careful history. It may be asserted that physiological albuminuria is rarely present to the extent above 1.20 per cent., while the presence of epithelial and granular casts speaks in favor of an organic disease. On the other hand, a clear cycle in the excretion of albumin is in favor of the functional character of albuminuria. Of especial interest, however, is the following statement of the author: "On the other hand, from my observations left-sided heart hypertrophy and abnormal tension of the pulse do not possess the importance from a point of view of differential diagnosis, which is frequently ascribed to them as indications of an interstitial nephritis."

In the great majority of his 111 cases further observations showed a great improvement in all the symptoms, including those relating to the heart and vessels.

Observations upon Koplik's Spots, Diazo-reaction, and Fever in Measles.—MULLER (*Münchener med. Wochenschrift*, 1904, No. 3, 51st Jahrg) had an opportunity to study an epidemic of measles involving

25 cases, which occurred in Marburg in the winter of 1902 and 1903. The epidemic spread very rapidly, as is shown by his curve, the cases increasing from 4 on the first three days to 18 on the fourth. The character of the epidemic was mild; complications occurred in 24 per cent. of cases. The mortality was 2.8 per cent. Six children died of bronchopneumonia. Most of the patients were four years old or under, the elder children having acquired immunity during a previous epidemic. In 166 of the Marburg cases Koplik's spots occurred 134 times, that is, in 81 per cent. An initial exanthem on the hard palate was observed 143 times, that is, in 86 per cent. of the cases. Since the great majority of all the patients were first brought to the polyclinic about the time that the exanthem began, it was impossible to say whether the Koplik spots preceded the appearance of the exanthem. In only 12 cases was it possible to follow the children with reference to this point from the incubation period to the outbreak of the disease. Of these 12 cases, Koplik's spots appeared 7 times simultaneously with the first rise of fever, that is, on the first day of the disease, 4 times one or two days after the occurrence of fever, and once the spots were absent altogether. In these 11 cases the Koplik spots appeared about 8 times from a half to two days previous to the initial exanthem, and 3 times the spots and exanthem occurred simultaneously.

The epidemic of measles, which ended in April, was followed in June and July by a little epidemic of rötheln. The diagnosis of rötheln was all the easier to make, as the greater number of the cases affected the same children who had recently recovered from measles. Fourteen cases of rötheln came under observation. In 6 of these Koplik's spots were definitely demonstrable. Nothing could be learned as to the time of the appearance of these spots, as all the cases were first seen with the full-blown exanthem. If one considers measles and rötheln as different diseases, it is evident that these cases prove that Koplik's spots alone are not diagnostic of measles.

A series of 10 cases were studied with regard to the diazo-reaction. Of these 10 cases, 8 showed the reaction first with the appearance of the exanthem, 2 half a day sooner. The intensity of the reaction increased with the duration of the continued fever and reached its highest point either with or soon after the maximum temperature. The reaction disappeared during the first days, at the latest six days after the disappearance of fever.

The fever curve of measles was also observed. In 12 cases where brothers and sisters of sick children contracted the disease the curve was followed from before the onset. Of these 12 cases, 9 showed the fever curve that is ordinarily given as a typical one in text-books. This type starts with a sudden rise. This is followed by a one to two-days' intermission, and then by a continued fever for several days. In 2 cases a more gradual remitting type of onset was seen, such as Heubner has described. In only 1 case did the fever rise suddenly without any previous remission.

Müller concludes his article, which gives an extensive review of the literature, as follows: 1. Koplik's signs are present in four-fifths of the cases of measles, and are frequently present on the first day of the disease. They are not, however, diagnostic of measles alone, as they were repeatedly observed in rötheln. 2. The diazo-reaction in the urine can be demonstrated almost always at the height of the disease. It occurs

usually with the appearance of the exanthem, and is not an early symptom. 3. In most of the uncomplicated cases of measles the fever curve shows a sharp rise at the beginning of the catarrhal stage. This rise is followed by an intermission, lasting one or two days, which, in turn, is succeeded by a rapid rise and continuous fever, lasting about four days, which falls usually by crisis. It is more seldom for the fever to rise by gradual remission or for it to start with a sudden unchecked rise.

SURGERY.

UNDER THE CHARGE OF

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Camphoric Acid as a Prophylactic for Urinary Fever.—FREUDENBERG (*Septième session de l'association francaise de urologie*, Paris, 1903) states that when he first practised the Bottini operation he frequently had cases that developed urinary fever—a complication alarming to the patient and disagreeable to the surgeon, as it varies in severity from a simple and relatively benign urinary fever to a true pyæmia in which the prognosis of necessity became extremely grave. Clinical experience has shown that the internal administration of quinine, salol, urotropin, methylene blue, etc., is absolutely without benefit, but that camphoric acid in three-grain doses, beginning some days before and continuing for some days after the operation, is an admirable prophylactic.

Intravesical Injections of Iodoform in the Treatment of Ammoniacal Cystitis.—FREUDENBERG (*Septième session de l'Association française de urologie*, Paris, 1903) states that while nitrate of silver and other agents have their principal action upon the bladder wall, the iodoform acts almost entirely in modifying the alkalinity of the urine, and, therefore, its use is not indicated in those cases of cystitis with acid urine nor in vesical tuberculosis. Its action is rapid. After one or more injections the masses of ropy pus and the ammoniacal odor disappear, the pain becomes less severe, and the desire to urinate frequently less urgent, while a cystoscopic examination will show that the mucous membrane is much less hyperæmic than before the injections were begun. The dose should be 0.3, suspended in glycerin, and then well diluted with some bland fluid, such as boric acid solution, and injected about every other day; but care should be taken to closely watch the patient, and at the first sign of intoxication the treatment should be stopped.

Wounds of the Stomach by Fire-arms.—FORGUE and JEANBRAU (*Revue de chir.*, 1903, No. 12), after an admirable and most complete review of the entire literature of this subject, state that every case demands immediate operative interference for its relief. This should consist in a median supraumbilical laparotomy, followed by an exploration of the anterior surface of the stomach, the liver, the neighboring coils of intestine, the spleen, all the accessible portion of the diaphragm, and the posterior surface of the stomach. All visceral wounds should then be closed by suture, the toilette of the peritoneum carefully completed, and then the abdominal wound closed after proper provision for drainage has been made.

Osteomyelitis of the Coccyx.—MONNIER (*Rev. de orthopédie*, 1904, No. 2) refers first to the interesting article by Grisel in the November issue of this JOURNAL on the "Primary Acute Osteomyelitis of the Vertebræ," in which he refers in detail to the forty-three cases of this disease which presented themselves for treatment at Kirmisson's clinic. In this series is included a note of six cases in which the sacrum was involved, and the seriousness of the disease may well be appreciated, for of these cases not one made a recovery. Monnier notes in detail one case in which the coccyx was involved, but which made a good recovery after operative interference.

Penetrating Wounds of the Heart; Suture; Death.—VINCE (*Jour. de chir. et annales de la soc. belge de chir.*, 1903, No. 7) states that the external wound was in the fifth left intercostal space, in the parasternal line, horizontal in its direction, and 2.5 c.m. long. Its borders were clean-cut, no bleeding externally nor bloody expectoration, no subcutaneous emphysema; the edges of the wound were closely approximated; the left side of the chest moved but little during respiration. On proceeding to the examination of the chest there was found dulness upward to the inferior angle of the scapula with all of the physical signs of a vast pleural effusion. An operation being decided upon, an incision was made with its superior border corresponding to the wound, the internal border corresponding to the left edge of the sternum and the inferior border corresponding to the superior edge of the eighth rib. This hinge-like skin-flap with the underlying cellular tissue was dissected backward. Then in the seventh interspace was found a gaping wound from which air and blood escaped with the respiratory movements. A musculo-osseous flap was then made, and the fifth, sixth, and seventh costal cartilages were cut. After turning them back the pleura was freely incised and found filled with blood, partially clotted. At each expiration the pericardium appeared in the wound. The lung was found retracted toward the vertebræ upon its hilum. The pleura was rapidly cleansed, and then the 2-c.m.-long wound in the pericardium was plainly visible. Upon separating the edges of the pericardial wound, it was found that there was a wound near the apex of the left ventricle, from which the blood "foamed" at each diastole. This wound in the ventricle was closed, using an intestinal needle and No. 2 silk, with three interrupted sutures, one of which perforated a coronary branch, necessitating its ligation. All hemorrhage being arrested, the pericardium was washed out and then closed with catgut sutures without drainage. The wound was then closed, and

the patient returned to bed, being much shocked. Salt solution and stimulants were freely used, but without avail, death following two days later.

Some points in this case would seem to merit further attention. 1. In regard to the difficulty of making a diagnosis. The most of the physical signs and symptoms presented by this case were simply of the presence of an intrathoracic hemorrhage, but the organ that was injured could not with certainty be discovered without operative interference. The only possible diagnosis was one of rapidly increasing hæmothorax, which demanded an immediate operation for its relief. 2. The patient bore chloroform anæsthesia very well. 3. The horse-shoe-shaped flap with the temporary resection of the costal cartilages proved valuable in that it widely exposed the field of operation. 4. In all cases of suture of the pericardium one should free the mediastinal portion of the pleura that is in contact with the pericardium, so that a separate suture of these two serous membranes can be made, which tends to limit the chances of their being eventually infected. 5. The pericardium was not drained, and it would seem to be best not to do so unless there existed some especial indication, for drainage is an essential factor in the production of pericardial, adhesion, and it does not prevent infection. The greater number of the fatal cases are those in which drainage was employed. However, drainage of the pleura is usually indicated by reason of the great ease with which this membrane becomes infected. This marked liability to infection is without doubt the greatest danger in all cases of cardiac wound.

THERAPEUTICS.

UNDER THE CHARGE OF

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Adrenalin in Gastrointestinal Hemorrhages.—Dr. M. H. Schlesinger has successfully treated two patients suffering from hemorrhage of the alimentary tract by adrenalin given internally. The first patient was a hæmophile, with severe intestinal hemorrhage. Six minims of a 1 : 1000 solution, given every hour, caused a cessation of the bleeding. In twenty-four hours the patient took 7½ drachms of the solution. After further administration of the agent, in connection with gelatin, a drop of blood obtained by puncture coagulated at once. The second patient suffered from essential purpura, with bleeding from various mucous membranes, especially that of the stomach. This was stopped by the administration of adrenalin given as in the first case. The author has employed the drug in various other forms of alimentary hemorrhage, with invariable success. Hæmoptysis, on the other hand, is not influenced by this treatment. Internal administration of adrenalin has no effect upon blood pressure.—*La semaine médicale*, 1904, No. 11, p. 86.

Tincture of Horse-chestnut in Hemorrhoids.—Dr. de Veney recommends the tincture of the horse-chestnut in all forms of this affection. Its first effect is to lessen the pain, which it does after a few doses, but if permanent results are to be accomplished the remedy must be continued for some time after the cessation of the pain. The dosage should be at least 10 drops in a little water before the two principal meals of the day, but the dose should be regulated according to the intensity of the symptoms. When these are severe and accompanied by marked turgescence of the tumors, 20 to 30 drops may be given, which quantity should be gradually lessened as the pain ameliorates. In cases with mucoid and dysenteric stools, blood, and tenesmus, the drug should be given with equal parts of tincture of aloes or in connection with a pill of $\frac{1}{10}$ of a grain of silver nitrate taken night and morning. For patients with intestinal atony and constipation equal parts of tincture of nux vomica should be given as an adjunct. The medicament may also be applied locally in an ointment, but its effects are not so marked when used thus as when given internally. Tincture of horse-chestnut is also useful in varices of the legs and in congestive disorders of the pelvis, such as inflammation of the neck of the bladder, prostatitis, proctitis, and uterine congestion.—*Journal de médecine de Paris*, 1904, No. 13, p. 126.

Electricity in Habitual Constipation and Mucomembranous Colitis.—M. Delherm has used in constipation a galvano-faradic current of over 50 milliampères with good results. In 46 out of 53 patients he has brought about regular spontaneous defecations and has modified the constipation, both quantitatively and qualitatively. Of 16 patients whose stools contained mucus this morbid condition disappeared in 13 and was ameliorated in 3. In all cases an increase of weight was noted. The results obtained lasted permanently in 36 of the cases. Cases of mucomembranous colitis were usually benefited by the treatment, the constipation disappearing and the mucus becoming less in quantity. M. Zimmern employs in membranous colitis a constantly varying continuous current with a long sinusoidal curve. With this he obtains satisfactory results, both immediate and remote. The membrane, the pain, and the constipation disappear in order. Dieting has no part in the treatment. Laxatives are given (castor oil or an enema), if necessary, about once in five days until the stools appear spontaneously. A regular hour for defecation is insisted upon, and at this time a small enema of cold water may be given, so as to excite the rectal reflex. The author does not consider that the electric current excites the intestinal musculature, but that it acts upon the vascular supply of the bowel through the solar system.—*La presse médicale*, 1904, No. 27, p. 215.

Sulphanilic Acid in Catarrhs of Mucous Membranes—M. Vautri states that this agent relieves acute laryngitis and causes the pain of otitis media to disappear rapidly. The neuralgic pains accompanying inflammations of the various mucous membranes rapidly disappear under its administration, but in true neuralgias the drug is useless. In chronic conditions it may be given for considerable lengths of time, but in these it is less effective than in acute inflammations. When taken in doses of from 15 to 20 grains per day for several weeks, it causes no digestive or other disturbance, except at times a slight diarrhœa. In

acute coryza a dose of ½ to 1 drachm is effective within two hours. The following is a good formula for the administration of the drug: Pure sulphanilic acid, 10 parts; sodium carbonate, 8½ parts; distilled water, 200 parts: from 5 to 10 drachms daily, preferably in two doses.—*Journal de médecine de Paris*, 1904, No. 11, p. 103.

A New Treatment for Asthma.—Dr. Saenger has reported good results from the treatment of asthma by means of respiratory exercises. He bases his theory upon the facts that the instinctively deep respirations during an asthmatic attack augment the dyspnœa. During the attack the lung is the seat of an acute emphysema and of an alveolar distention which result in a diminution of the movements of the thorax. The deep inspirations made by the patient increase the quantity of residual air, and this also increases the immobility of the chest wall and exaggerates the dyspnœa. To combat this the patient ought to inspire as little air as possible and to make his expirations as long and as slow as he is able. Few and shallow inspirations and long and effortless expirations are to be attempted. The patient is advised thus, and is told that there is no danger of asphyxia. The slow and prolonged expiration is difficult, and the patient is told to whistle for three or four seconds before taking a shallow inspiration, or to count in a loud voice up to five and then inspire and to continue this scheme for ten or fifteen minutes. Certain cases are able to count as high as ten before inspiring. Another advantage of the method is that it takes the patient's mind from his dyspnœa. Between attacks it is advisable for the patient to practise the procedure daily for fifteen minutes. With practise it becomes possible to count even to forty before taking an inspiration. The author has employed the treatment in 11 cases, in 9 of which it has achieved remarkable results; the habitual respiratory oppression was greatly lessened or disappeared entirely, the intervals between attacks were lengthened, and at the same time, the bronchitis and emphysema were favorably influenced.—*Münchener medicinische Wochenschrift*, 1904, No. 8, p. 335.

The Treatment of Alopecia Areata.—M. Charmeil recommends the following treatment: In marked cases the entire scalp should be clipped. Pure acetic acid should be applied to the bare areas by means of a small cotton swab. This should be quickly applied and the seat of the application at once dried with cotton. The skin immediately becomes blanched, but within a few days an intense redness appears and sometimes a small blister; after several days the skin resumes its normal appearance. The patient should be given a prescription, which is to be applied with friction every two or three days, such as follows: Ether, 6 drachms; chloral hydrate, 15 to 60 grains; crystalline acetic acid, 8 to 30 grains. This maintains the counterirritation of the skin. Other counterirritants, such as chrysarobin, tincture of iodine, croton oil, or solutions of carbolic acid, may be employed. In rebellious cases some vesicant in the form of a plaster may be applied, and the raw surface touched with silver nitrate solution, 1 : 15. Care should be exercised not to blister so deeply as to cause cicatrices. The whole scalp should be shampooed twice a week and a solution analogous to the following rubbed in: Alcohol, 90 per cent., 300; tincture of lavender, 100; tincture of melissa, 100; mercury bichloride, 0.006; tincture of cantharides,

15; chloral hydrate, 5; castor oil, 2. In addition, the employment of massage, vigorous brushing, and faradization are useful.—*Journal de médecine de Paris*, 1904, No. 14, p. 138.

Arsenous Acid in Sleeping Sickness.—M. A. LAVERAN states that arsenous acid, which has given favorable results in the treatment of this disease, will cause the trypanosoma to disappear temporarily, at least, from the blood of infected rats. The proper dose is one part for each 20,000 of the animal's weight. Smaller dosage than this produces an incomplete effect or none at all. A solution containing 1 gram of arsenous acid and the same quantity of sodium carbonate to 500 grams of distilled water is used. Possibly this treatment might be applicable to human beings infected with the parasite in the phase of the affection which precedes the appearance of nervous disturbances. It is better to give large doses at intervals than smaller daily doses, as has hitherto been the custom.—*La semaine médicale*, 1904, No. 9, p. 68.

Treatment of Neuralgia.—DR. BASTIE reports remarkable results from the following treatment. He uses extract of valerian, 3; hyoscyamine, 0.045, or extract of hyoscyamus, 0.75; morphine hydrochlorate, 0.15. These formulæ are made up in pill form, and one pill is given at nine or ten o'clock in the evening and a second a half hour later. A third is given at five in the morning and a fourth at eight. These are sufficient to relieve the pain completely. If there is a recurrence the patient may take a pill each morning and evening for eight days. All neuralgias, when uncomplicated, yield to this treatment. Between the attacks 15 grains of quinine are administered twice a day. When there is congestion of the involved nerve the treatment is supplemented by leeches applied at the point of emergence.—*Revue francaise de médecine et de chirurgie*, 1904, No. 7, p. 161.

OBSTETRICS.

UNDER THE CHARGE OF

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Induced Labor, with Especial Reference to the Permanent Results for the Children.—LOREY (*Archiv für Gynäkologie*, Band lxxi., Heft 2, 1904) contributes an interesting and instructive paper upon this subject. The most frequent indication for the induction of labor is contraction of the pelvis, and Lorey reports the results of 100 cases.

The most frequent variety of contracted pelvis was the flat rachitic; next in frequency, the justo-minor, and after that the irregularly contracted pelvis. Of these 100 children, 74 were born living, or 74 per

cent. Of these 19 per cent. died during the first ten days of life; 60 per cent. left the hospital living. The subsequent history of 56 children was obtained after they left the hospital, and 71.5 per cent. of these children survived the first year. Of 51 illegitimate children, 78.5 per cent. lived through the first year.

These operations were performed upon 83 women, 88 per cent. of whom recovered without fever. One patient died of septic infection; the mortality of the mothers was 1.2 per cent.

Observation shows that the induction of labor in contracted pelvis is most successful in the interests of mother and child if it be not too long postponed and if the pelvis is but slightly contracted. In the interests of the child it should not be induced before the thirty-fifth week of gestation, and it must be considered as fatal to the child before this time as is craniotomy.

Pregnancy was also interrupted in thirty-seven cases because of some disease of the mother. Fourteen of these cases had eclampsia, 6 nephritis, 3 disease of the heart, 6 placenta prævia, 4 obstinate dyspnœa, 1 goitre, 2 polyhydramnios, 1 carcinoma, and 1 infection of the bladder produced by pressure of the head upon the urethra.

The mortality among these children was 36.8 per cent., while 63 per cent. left the hospital living. So far as could be traced, 70 per cent. of these children died during the first year of life, while but 30 per cent. survived the first year. It was estimated that in all but 15.8 per cent. of the children remained alive at the end of the first year.

Lorey would not advise the induction of labor in contracted pelvis where the internal anteroposterior diameter was 7 cm. or less. Where the internal anteroposterior diameter varied from 8 to 10 cm. induced labor is indicated when the patient's history shows a marked disproportion between the head and the pelvis. In these cases the operation should be done before the thirty-sixth week. The use of bougies or elastic dilators is advised. In cases where much interference is practised, the prophylactic injection of antistreptococcic serum is recommended. In all serious diseases affecting the mother, labor should not be induced in the interests of the child.

Nephrotomy in Eclamptic Anuria.—In the *Zentralblatt für Gynäkologie*, No. 15, 1904, SIPPEL reports the case of a multipara, aged thirty-five years, who had eclampsia and, after the delivery of the child, anuria, which did not yield to treatment.

Upon autopsy, a condition of both kidneys was found resembling glaucoma. The case seems one in which incision of the kidney or decapsulation might have given good results.

Labor Complicated by Fracture of the Pelvis.—In the *Archiv für Gynäkologie*, Band lxxi., Heft 2, 1904, BOSSE describes the case of a patient who had once tried to commit suicide by throwing herself from a window upon a pavement. She had fallen upon the left femur and ischium. The patient was pregnant at the time, had incomplete abortion, which was terminated by curetting. She had incontinence of urine and feces, with atrophy of the lower extremities, and after four months' treatment was able to leave the hospital, a positive diagnosis of fracture of the pelvis never having been made. The patient made a gradual recovery and was able to sit and walk without pain.

She was afterward admitted pregnant and at full term, and, as delivery failed, hysterotomy was performed. She made a good recovery.

On examination she was found to be markedly rachitic, with an external conjugate of 18.5 cm.; the left tuberosity of the ischium was 1 cm. higher than the right. The diagonal measurements of the pelvis were unequal, the conjugate diameter being 8 cm. and the true conjugate 5.5 cm.

A radiogram of the pelvis was obtained, when the right half was found normal. The left half of the pelvis seemed to be higher than the right, and the pelvic girdle was broken by three fractures. One had extended through the left sacroiliac synchondrosis, one horizontally through the pelvis, and a third between the ischium and pubes. An exostosis had developed, and the sacrum seemed to be much shortened. There had also been injury to the last three lumbar vertebræ. The case would be considered by some writers upon the subject as a double vertical fracture.

Treatment of Retroversion of the Gravid Uterus.—Herman (*British Medical Journal*, April 16, 1904) reviews the pathology of this condition, and quotes the statistics from the London Hospital and from St. Bartholomew's Hospital. In the former institution, from 1885 to 1893, there were 79 cases of retroversion of the pregnant uterus. In 74 cases, 40 showed spontaneous ascent of the womb when the patient was kept recumbent and the bladder emptied. In 33 patients the uterus was manually replaced. Two cases aborted; in both the uterus had been replaced. Two died from toxæmia. In 1 case a water-bag was used to replace the uterus, and it is questionable whether it produced an effect.

At St. Bartholomew's Hospital, from 1881 to 1892, there were 42 cases, in 25 of which the bladder was emptied and the uterus easily replaced. In 2 cases attempts at reposition failed, but the bladder was frequently emptied, and the uterus afterward assumed a normal position spontaneously. In 2 cases abortion was induced, and 3 cases aborted spontaneously. Two died from the effects of retention of urine on the bladder and kidneys.

In these two hospitals there were 115 cases, with 5 abortions, or 1 in 23. This is about one-fourth of the usual frequency of abortion.

Herman believes that practically the only danger from retroversion of the gravid uterus results from the retention of urine. He considers the one necessary treatment the frequent use of the catheter.

He has never seen a case of retroversion in the gravid uterus where the womb could not be pushed up. He believes that the finger carried into the rectum is most efficient in bringing about this result. He sees no occasion under any circumstances to resort to abdominal section.

Death from Pulmonary Clot following Operation for Ectopic Gestation.—Hind (*British Medical Journal*, April 16, 1904) reports the case of a multipara who was operated upon while in a desperate condition for ruptured ectopic gestation. There had been free hemorrhage with the discharge of much blood into the abdomen. Eleven days after the operation the patient seemed quite well, except that the breathing was more rapid than normal and the pulse somewhat feeble. Without apparent cause she suddenly collapsed and died.

At autopsy the wound was healed, there was no sign of septic infection, the peritoneum was healthy, and the stump of Fallopian tube was firmly closed by the silk ligature. The pulmonary artery contained a large clot, laminated on section, and hollow in parts.

GYNECOLOGY.

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Treatment of Cervical Metritis.—RICHELOT (*La gynécologie*, 1904, No. 2), reviewing the result of his treatment of glandular endocervicitis with caustics, admits that the results as regards subsequent cicatrization have not been satisfactory, although he claims that after the lapse of six months or a year the cervix will be restored to a normal condition.

Epithelioma Developing from the Stump of a Polypus.—CROISIER (*La gynécologie*, 1904, No. 2) reports a case of intrauterine polypus, the stump of which was situated so high up in the uterine cavity that he could not excise it per vaginam. Fragments of the growth removed for examination were pronounced by the pathologist to be epitheliomatous, so that he decided to extirpate the uterus. As the cervix appeared to be healthy, supravaginal amputation was performed instead, the patient making a good recovery.

Examination of the specimen showed that the neoplasm was a fibromyoma, the stump of which showed well-marked cancerous infiltration involving the subjacent muscular tissue. The writer properly questions the wisdom of leaving the cervix, under the circumstances.

Referring to the supposed infrequency of cancer and fibromyoma in the same uterus, he reports four cases in which the two conditions were associated. In his opinion a fibroid uterus forms a favorable soil for the development of malignant disease, probably due to the endometritis which is generally present.

Radical Cure of Cancer of the Uterus.—BAROZZI (*La gynécologie*, 1904, No. 2), after analyzing the statistics of abdominal and vaginal extirpation of the cancerous uterus, asks how long a time should elapse before a patient is pronounced cured. He concludes, with Winter, that five years should be regarded as the limit, though recurrence has been noted as late as seven or eight years after operation.

Myomectomy versus Hysterectomy.—BATIGNE (*La gynécologie*, 1904, No. 2) concludes a paper on this subject, with the statement that the conservative operation should be confined to cases of single tumors in

young subjects, especially when the patient has expressed a strong desire to have the uterus preserved in the hope of future pregnancy; also in cases in which the presence of the neoplasm in a pregnant uterus is a menace to the continuance of pregnancy and the subsequent delivery.

Cysts of the Clitoris.—CAZIN (*La gynécologie*, 1904, No. 2) reports a case in which he removed a large pedunculated tumor which grew from the prepuce of the clitoris. It was polycystic, the cysts being lined with prismatic epithelium and containing a viscous fluid. In the discussion of this paper before the French Surgical Congress similar cases were reported by Témoin and Tédenat.

Cancerous Degeneration of a Uterine Fibroid.—FRANCHOMME (*Soc. des sciences méd. de Lille*) reports the case of a patient, aged sixty-four years, with metrorrhagia, who several years before had had a uterine polypus removed. On entrance to the clinic a large bleeding neoplasm presented at the os externum. The diagnosis of epithelioma was made and the growth was removed. Microscopically it was found to be composed of fibromuscular tissue filled with masses of pavement epithelium.

The writer comments on Richelot's advice always to perform total hysterectomy, in order to avoid possible cancerous degeneration of the cervix.

Congenital Anomaly of the Fallopian Tubes.—RONSSE (*Annales de la soc. de méd. de Gand*) reports the case of a woman, aged twenty-six years, who had menstruated regularly since the age of sixteen, though the periods were scanty and painful. She had been married six years without conceiving. The uterus was normal, the os being small. Divulsion and curettement were performed without the desired results. A year later the abdomen was opened on account of persistent pain and evidence of ovarian disease. Both ovaries were removed for cystic degeneration. The tubes were normal as far as their distal ends, where they terminated in a cul-de-sac, both fibrinated ends being wanting. There was no evidence of inflammation in or around the tubes.

The writer regards this anomaly as a proof of the dual origin of Müller's ducts, the proximal part of the tube formed by the invagination of the peritoneal epithelium being absent, while the distal portion developing from the Wolffian canal was normal.

Vaporization of the Uterus.—HAUTKE (*Zeitschrift für Geb. u. Gyn.*, Band xlix., Heft 2), in a recent discussion of this subject before the Berlin Obstetrical Society, stated that this method of treatment was not free from danger, since he had known of two fatal cases. The indications, he believes, are limited, being confined to those cases in which all other methods of treatment had failed, especially untractable climacteric hemorrhages. The writer always satisfies himself that he has not to deal with an atrophic or thin-walled uterus before introducing steam into it, and is sure that ample dilatation of the cervix is maintained. Submucous fibromyomata form a contraindication, and he never employs this method of treatment in young subjects.

Mackenrodt, in continuing the discussion, held that vaporization was a distinct step backward in gynecological therapeutics, to be included in the same class with cauterization with chloride of zinc. He had been obliged to extirpate several uteri for hæmatometra due to cicatricial contraction of the cervix following such treatment. Climacteric hemorrhages, if not due to malignant disease, are referable to arterial sclerosis. How this condition could be cured by destruction of the endometrium he could not understand. Total extirpation of the uterus is not only safe, but more scientific in cases of recurrent bleeding. With submucous fibroids repeated curettement is better than vaporization, while if the hemorrhage is due to adnexal disease the latter treatment is certainly useless.

The speaker did not find that the great expectations which had been held in regard to the intrauterine use of steam had been realized, but in isolated cases of hæmophilia he acknowledged that it might be indicated, though he had never met with one himself.

Czempin said that he had used steam at a temperature of 100° to 101° C. for three minutes with marked benefit, and had never seen stenosis follow. He had always made it a practice, however, to pass sounds for six weeks afterward, in order to insure patency of the cervical canal. He disagreed with Mackenrodt with regard to arteriosclerosis as a cause of climacteric hemorrhages, and in any case the effect of vaporization was to contract bloodvessels and to cause shrinkage of the uterine parenchyma, as well as the endometrium.

Appendicitis Complicated by Ectopic Gestation.—Temoin (*La gynécologie*, 1904, No. 2) reports two cases of acute appendicitis associated with extrauterine pregnancy. In both the latter condition was not suspected, as the symptoms pointed clearly to perforation of the appendix. In both it was necessary to resort to median laparotomy, as the ordinary lateral incision did not give sufficient room. The diseased appendix and ectopic sac were fused together. One operation was performed on the fourth and the other on the fifth day after the initial attack, vaginal drainage being employed. Both patients recovered.

Endothelioma of the Cervix Uteri —Kirchgessner (*Zeitschrift für Geb. u. Gyn.*, Band xlix., Heft 2) concludes an article on this subject as follows: Contrary to the opinion of Gebhard, young subjects are more apt to be attacked with this disease than old. Endothelioma may develop in nulliparæ as well as in multiparæ. The clinical symptoms are the same as those of cancer, *i. e.*, hemorrhage and foul discharge. The neoplasm is usually nodular, of variable consistence. No case of recurrence after removal has been reported, in spite of Burst's statement that endothelioma is known to recur locally. It grows slowly and has a limited power of metastasis. A radical operation should be performed as soon as the diagnosis is confirmed microscopically.

Tubercular Infection of Ovarian Cysts.—Prusmann (*Archiv. für Gynäkologie*, Band lxviii., Heft 3) affirms that no genuine case of primary tuberculosis of the ovary has yet been described. In the case reported by him an ovarian cyst containing tubercles was removed, without any trace of the disease elsewhere in the pelvis or abdomen. In this instance infection may have occurred through either the genital tract or the lymphatics, *i. e.*, by coitus. The finding of giant cells in

the lymphatics of the broad ligaments led to a belief that these latter were the channels of infection. Cornet and Jani have shown what a prominent role coitus plays in the transmission of the disease, since the tubercle bacilli in the semen are especially virulent.

Fibromyomatous Lipoma of the Uterus.—SEYDEL (*Zeitschrift für Geb. u. Gyn.*, Band l., Heft 2) describes a uterus which was extirpated for malignant adenoma of the vagina. A small intramural growth was found at the fundus, which presented the appearance of an ordinary fibromyoma, but on section was found to be filled with masses of fat. Only ten other cases of uterine lipoma have been reported.

The origin of the fat has never been satisfactorily explained. The writer leans to the theory of inclusion of lipoblasts in embryonic life, thus agreeing with Merkel and Knox.

OTOLOGY.

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Precautions against Injury from Unsuccessful Attempts at Extraction of Foreign Bodies from the Ear.—LEUTERT (*Archiv für Ohrenheilkunde*, vol. lxi., Nos. 1 and 2) draws attention to the dangers attending the attempts at extraction of foreign bodies impacted in the external auditory canal when these efforts are made under the conditions of imperfect knowledge of the parts dealt with, the use of improper instruments, or the lack of proper illumination of the operative field.

A boy, aged four years, had, several days previously, thrust a pea into his left ear. The physician who was called attempted to remove the foreign body by means of a hair-pin and without the aid of proper illumination, ceasing his attempt only after causing both considerable pain and a sufficient bleeding to obscure the field.

On examination the right ear was found to be normal both as to appearance and hearing power.

The lining of the left auditory canal was much swollen, and in the meatus were blood and a trace of thin purulent discharge.

On syringing with a normal salt solution the fluid ran freely from the left nostril, and as symptoms of pain and fever were wanting, the ear was lightly bandaged and the patient told to return at the end of eight days unless unfavorable symptoms made an earlier visit advisable.

Eight days later the swelling of the canal had so far diminished as to make an inspection of the drumhead possible, and there was found a large perforation, including almost the whole of the drumhead anterior

to the malleus, which was in normal position. The presence of the foreign body was not determined.

At the end of another week the further subsidence of the swelling in the canal revealed the perforation in its full extent and a rounded foreign body lying within the middle ear upon the tympanic floor. Attempts at removal by syringing failing, because the fluid, instead of returning escaped through the Eustachian tube and nose; the auricle was reflected forward and the pea easily extracted by means of a blunt hook. The healing of the post-auricular wound was effected without incident, but treatment of the suppuration of the middle ear had to be subsequently continued.

From this and similar experiences, coupled with a review of the literature of the subject, the writer draws the following conclusions:

1. In all early cases, seen at first hand, the primary attempt at extraction should be made with the syringe, and should the first attempt fail, this treatment should be successively repeated, unless it is found that, in consequence of a perforation of the drumhead and escape of the fluid through the Eustachian tube, this measure is negatived.

2. When it has been definitely determined that removal of the foreign body by means of syringing is impossible, instrumental manipulation may be resorted to, but only under conditions of good illumination and with instruments which may be passed beyond the foreign body, between it and the canal wall, without injury to the deeper seated parts. If instrumental manipulation is found to be ineffectual without danger to the soft parts, the auricle should be reflected forward and the body extracted.

3. In the event of previous attempts at extraction which have resulted in injury to and swelling of the canal walls, this swelling should be allowed to subside before further attempts at extraction are made. In the case of symptoms which demand immediate interference and extraction, either through the lumen of the canal or post-aurally, this should preferably be done under an anæsthetic.

Rupture of the Drumhead Caused by a Blow upon the Ear.—MENIERE (*Archives Internationales*, vols. xvii., No. 3) relates a case of a young man, aged twenty-five years, who received a blow upon the left ear in boxing, the hand of his adversary being covered with the ordinary soft leather boxing-glove. The blow was followed immediately by a sensation of sharp pain in the depth of the ear and by slight vertigo. Examination of the ear, one hour later, showed a rupture of the drumhead about 4 mm. in diameter in the anterior-superior quadrant, partly concealed by a few drops of blood. The subjective symptoms were of a very moderate character, but little pain and a slight tinnitus.

The treatment consisted in the application of a warm douche of weak boric acid solution for three or four minutes and the subsequent stopping of the canal with a firm pledget of absorbent cotton; furthermore, the patient was advised, in the event of a desire to blow the nose, to abstain from the use of a handkerchief and to clear the nose by blowing gently with only one nostril closed at a time. In addition, the patient was directed to insufflate a warm boric acid solution.

Three days later the opening in the drumhead was closed by a clot, and on the eighth day after the accident cicatrization was complete and the hearing absolutely normal; there remained only the tinnitus as a

reminder of the injury, and this symptom also disappeared entirely at the end of fifteen days.

Traumatic ruptures of the drumhead, except such as are the result of direct violence, are most common among artillerymen and others following occupations which expose them to loud concussions. Cases of concussion rupture from a direct blow upon the outer ear are much less common, but the writer cites a similar case in which a slight buffet upon the auricle resulted in a rupture of the drumhead extending over three-quarters of its surface; treatment of the same character as that above given was employed, but the case was much more slow in healing, it being at least a month after the accident before this result was attained.

As the result of his experience in similar cases, the writer advises for treatment: 1. Disinfection of the parts by the use of peroxide of hydrogen. 2. Firm stoppage of the canal. 3. Avoidance of inflation of the middle ear.

OPHTHALMOLOGY.

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Ligation of the Lacrymal Canal to Prevent Infection following Cataract Extraction.—QUACKENBOS (*Boston Medical and Surgical Journal*, March 31, 1904) reports two cases of ligation of the lacrymal canal to prevent infection following cataract extraction. The usual preparations for cataract extraction were carried out. Cocaine was used, then the contents of the mucocele were squeezed out and the eye washed with corrosive, 1:5000. A small probe was inserted into the upper punctum and a suture passed around the canal from the inside of the lid out. This was repeated on the lower lid. The sutures were passed 2 mm. or 3 mm. from the punctum and were tied quite firmly. The usual operation for cataract was done and the healing was without incident. The stitches were removed at the end of two weeks in the first case, and nine days in the second case. The author believes that the stitches should be removed as soon as the corneal wound has healed firmly. He claims that the advantages of this method are "its simplicity, the ease with which it can be done, its freedom from pain, that it can be done at the time of the operation, and that it can be used even in doubtful cases."

The Epidemic of So-called Trachoma.—ALGER (*New York Medical Journal* and *Philadelphia Medical Journal*, April 9, 1904) makes some appropriate observations upon the scare on the subject of trachoma from which the people of New York, and, to some extent, of the whole country, have been victims. Beginning with the ruling of the United States immigration authorities, anxious to find some excuse for prohib-

iting the entrance into the country of so-called undesirable classes of immigrants, it has spread to the schools, from which thousands of children have been excluded because of their supposed infection with a dangerous contagious disease. Many of those who fomented the agitation were not altogether altruistic; some were influenced by race prejudice; others were eager for increased appropriations for their dispensaries.

Alger insists upon the great importance of distinguishing follicular conjunctivitis from trachoma. The former is a trivial matter. True trachoma is a real scourge leading to unending discomfort and suffering and often resulting in the most serious consequences to the sight. There can be no doubt that the vast majority of the thousands of children who were affected had simply the mild disease. The heroic measures with which many of them were treated were both cruel and useless. These views are not new. The best authorities fully endorse them, but they should be borne in mind and acted upon by ophthalmic surgeons who have to give an opinion when cases of suspected trachoma are brought to their notice.

Ethyl Chloride as a General Anæsthetic in Eye Work.—STEPHENSON and CHALDECOTT, London (*The Ophthalmoscope*, April, 1904) highly recommends this agent as being especially useful in eye work. It has several distinct advantages over all the older anæsthetics. It is easy to give. Anæsthesia is quickly reduced and its effects pass away rapidly. Vomiting is not common. Cyanosis or jactitation do not occur. A single dose is administered, which will certainly within a few seconds induce the necessary anæsthesia, but which is not sufficient to kill. If the operation is more protracted it is easy to administer more ethyl chloride or to continue the anæsthesia by means of chloroform. It is especially useful in permitting thorough examination in young children with intense photophobia and in the exquisitely sensitive corneas of patients suffering from gonorrhœal ophthalmia. Under its influence lacrymal probes can be passed, chalazia extirpated, canthoplasty performed, trachomatous granulations expressed, the anterior chamber tapped, corneal ulcers cauterized, lens and secondary cataracts needled, and the recti divided, etc.

Cases of Hydatid Cyst of the Orbit.—MARSHALL, of London (*The Ophthalmoscope*, April, 1904), reports an instance of this rare disease. The patient was a girl aged five years. The right eye had turned for about eighteen months; between the ball and the inferior and outer margin of the orbit a tumor the size of a muscatel grape, apparently fluctuating, was situated. The movements of the globe were free, although less than normal, especially restricted outward and downward. The eye appeared to be healthy and the pupil active; vision doubtful. The growth was removed in its sac. The cyst was found to be one-and-a-half inches in diameter, with all the characteristics of an hydatid cyst. There were no echinococcus heads in it, as is usually the case, for heads and hooklets are noted in only a small minority of cases of human echinococci. These cases are exceedingly rare. Prior to 1895 only 45 cases had been published. Since then others have been reported. There is one other situation, however, in which it is still less common to find the cyst, and that is in the eyeball itself. Marshall knows of only 3 cases of this condition.

PATHOLOGY AND BACTERIOLOGY.

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Is Human Tuberculosis and Tuberculosis of Domestic Animals Caused by the Same Variety of Micro-organism, Namely, the Bacilli Koch? (Internationaler Kongress für Hygiene in Brüssel, 1903.)—The results of the discussion upon this subject as given by LIGUIERES (*Cent. f. Bakt. u. Parasitenkunde*, 1904, Bd. xxxiv. p. 427) are that from the tuberculous lesions of man and animals specific bacilli can be isolated, which, though belonging to the same group of micro-organisms, yet possess sufficiently different characteristics to stamp them as distinct varieties. The bacillus of avian tuberculosis differs from that of human tuberculosis, both as regards cultural properties and pathogenicity. The bacillus of human tuberculosis differs from that of bovine tuberculosis in various and constant pathogenic criteria. Whereas the bovine bacillus produces a more or less general tuberculosis when injected into cattle, the bacillus of human tuberculosis when inoculated in the same manner calls forth only a local transient reaction, which heals and leaves no tuberculous infection demonstrable through lesions, presence of bacilli, or tuberculin reaction. In general, one finds the bacillus of avian tuberculosis in birds, the bacillus of human tuberculosis in man, and the bacillus of bovine tuberculosis in cattle, although the latter variety may exceptionally be demonstrated in man, especially in cases of primary intestinal tuberculosis. When the cases of accidental infection of man are considered, either through wounds or through ingestion of virulent milk from a cow which is the subject of tuberculous mastitis, the proof of the possibility of infection of man by means of the bovine tubercle bacillus is at hand. For this reason, it would be a great mistake to abandon the well-organized fight against bovine tuberculosis. This is of special importance, since tuberculosis is constantly increasing among cows.

On the Action of Hæmolysins in the Body.—FUKUHARA (*Ziegler's Beiträge*, 1904, Bd. xxxv. p. 434) studied the effects of intraperitoneal, subcutaneous, and intravenous injections of heterohæmolysins in rabbits, guinea-pigs, rats, pigeons, and chickens. These injections were frequently followed by a slight elevation in temperature, hæmoglobinuria, and evidences of marked renal disturbances. In one guinea-pig there was a bloody diarrhœa. Besides the solution of the hæmoglobin of the red blood corpuscles, other evidences of degeneration and signs of regeneration rapidly made their appearance in the circulating blood. Icterus was occasionally noted. Large doses of the hæmolytic sera were quickly fatal. Death was referred to the toxic action of the sera

upon various kinds of cell protoplasm. In the less acute or chronic cases the internal organs showed coagulation of the blood with plugging of the capillaries and small vessels by thrombus masses, hemorrhages noticeable particularly in the heart muscle and kidney, ulcers in the stomach and intestines, hæmoglobinæmia, and pigmentation of various organs. It was thought that the hemorrhages in the heart and cortex of the kidney were due to a thermolabile toxin of the hæmolytic sera, since they did not occur if heated sera were used. Small foci of necrosis were frequently found in the liver. In a severe case degeneration of the bone-marrow was found, while with milder intoxications proliferative changes of the bone-marrow cells were noted. The erythrocytes were particularly affected; the eosinophiles appeared very resistant. The injection into an animal of foreign erythrocytes and subsequent intravascular solution of these cells called forth a series of changes much like those following injections of heterohæmolysins. Bile may have the same destructive effect as hæmolysins upon the blood. The author concludes that the action of a cytolytic serum is not specific. Hæmolytic serum injures not only red blood corpuscles, but heart muscle, liver cells, and kidney cells.

Demonstration of the Bactericidal Reaction in the Blood Serum of Typhoid Fever Patients.—STERN and KORTE (*Berl. klin. Wochen.*, 1904, No. 9, p. 213), by using a method devised by Neisser and Wechsberg, have measured the bactericidal power of the blood serum of typhoid fever patients and of normal individuals. To fixed quantities of fresh unheated rabbit serum and a dilution of a twenty-four-hour bouillon culture of typhoid bacilli varying amounts of heated typhoid serum were added. After the mixture had remained at 36.5° C. for three hours the whole was plated. The authors find that almost complete bacteriolysis takes place, even when typhoid serum is used in very high dilutions. In a few cases the serum, when diluted 50,000 times, is still active. Sera from persons who have not had typhoid fever possesses a much lower bactericidal value, and usually is only effective in dilutions of 1 : 200 or thereabouts. No relationship can be made out, either between the severity of the disease or the tendency to relapse and the bactericidal value of the serum. Neither does there appear to be any direct connection between the agglutinating power of the serum and its bactericidal action. Sera diluted beyond the agglutinating point are still bactericidal. The authors suggest that this method of determining the bactericidal value of the blood serum may be of clinical value in the diagnosis of typhoid fever, especially when the Widal reaction is delayed in its appearance.

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"TWO THOUSAND OPERATIONS FOR APPENDICITIS,"

WITH DEDUCTIONS FROM HIS PERSONAL EXPERIENCE.

By John B. Murphy, A.M., M.D.,
of Chicago.

It seems to me that a retrospective consideration of the subject of appendicitis might be of value to the general practitioner and the surgical specialist, as well as to the occasional operator in this disease. It would be useless to tabulate such a large number of cases unless all of the phenomena of etiology, symptomatic manifestations, clinical course, technical procedure, pathological conditions, and final results were included. This would mean an enormous labor from which, I believe, there would be no adequate return. The first operation, in its modern sense, was performed by me March 2, 1889. The two-thousandth was completed July 22, 1903.

I will refrain from going into the history of the struggles of the pioneers in the operative treatment of appendicitis. There is no procedure in surgery where the battle was so fierce and so continuous and where the statements of the uninformed were so personal, so galling, and so unjust as in the contest for and against early operation in acute infective appendicitis. Looking backward one can scarcely comprehend how a so-called intelligent profession was so slow in accepting the overwhelming force of numbers and facts, which could not be altered by theory or speculation. It is, however, but a repetition of the past and an index of the future; the medical profession, as a body, always has preferred to theorize and dream rather than analyze, investigate, or accept facts. This is particularly true of the pathological conditions of internal organs, and what could be said regarding the attitude of the profession

toward the diseases of the appendix in March, 1889, can be said to-day of diseases of the stomach, the pancreas, and, with little reserve, of the kidneys.

The diversity of opinion expressed as to the presence or absence of pus in acute, infective appendicitis, in the discussions in 1889, 1890, and 1891, is most interesting reading for the student of medical progress. Practitioners whose cases recovered from the attack insisted that they were catarrhal inflammatory processes and recovered without the formation of pus, notwithstanding the evidence produced by every operator of that time that pus was present in all of the acute infective cases operated in the early stages—now a generally recognized fact. Every one recalls how reluctantly the advocate of the soothing, death lullaby of the opium treatment vacated his position, and how equally persistent and belligerent was the advocate of the death-groaning calomel and castor oil participant; the still unconquered, nine-lived procrastinator has not yet capitulated, each and every one of these standing out against the most convincing presentation of pathological phenomena.

Surgical Anatomy. The appendix, from a surgical standpoint, can be considered as located almost universally in the right lower quadrant of the abdomen, between a line drawn from the umbilicus to the symphysis and one drawn from the umbilicus to the tip of the eleventh rib on the right. The base of the appendix is usually found a little above a line drawn from the umbilicus to the anterior superior spinous process of the ilium and about two-fifths of the distance from the process (McBurney's point). In inflammatory conditions the appendix is usually found extending downward from this point. In children it is usually higher up. It may even approximate the costal arch and become attached to the margin of the liver or gall-bladder, or rest behind the caput coli. Once I found it between the liver and the abdominal wall. Below, it may be closely adherent to the inguinal tract, hanging over the margin of the pelvis; or, indeed, be found in the vesicorectal or Douglas' pouches. When the point of extreme sensitiveness cannot be determined in the usual position, examination of the loin and rectal and vaginal examinations should never be overlooked, as in about 5 per cent. of the cases I have found the appendix in the pelvis, and in a large proportion of these the abscess was entirely confined to the pelvis, not always to the right half of the pelvis, but filling in the entire pelvis, the vesical tenesmus and urinary retention indicating its location. In only two cases did I find the appendix to the left of the middle line. Once it was adherent to the left tube and the second time to the transverse colon. It was rarely found behind the peritoneum, although abscesses in the retroperitoneal space, from acute appendicitis, were not rare, due to perforation and not to malposition of the appendix. It is many times embedded in the wall of the caput coli. When found in that position in the

intermediate operations I have always considered it, not an anatomical anomaly, but a pathological sequence. In the intermediate operations, as well as in the acute stage, it is occasionally found attached to the ileum. Twice I found it strangulated and gangrenous in femoral hernia, and a number of times, in the acute and intermediate operations, in inguinal hernial sacs. The presence of acute infective appendicitis should be suspected in all right-sided hernias, where there is rapid elevation of temperature, with nausea and vomiting, shortly after the manifestation of strangulation, as simple intestinal strangulation in a hernial sac never gives a primary elevation of temperature. I have never found the appendix in an umbilical hernia.

The length of the appendix varied greatly—from three-quarters of an inch to six and three-quarter inches. The mesoappendix is from two and a half to four inches in length. In pathological conditions it may be entirely absent; that is, the appendix may be adherent to the intestine or to the abdominal wall. The mesoappendix is attached for about two-thirds of the length of the appendix; occasionally it is of enormous thickness, containing large deposits of fat. Many times the tip is adherent and an opening exists between the tip and the mesentery. I have had four cases of intestinal obstruction through this opening.

The proximal end at the valve of Gerlach is usually the smallest portion of the lumen. In acute infections of the mucosa, this opening becomes occluded from the œdema, producing retention of the infective material, as manifested by the acute primary colic and reflex primary nausea. The most severe infection and necrosis of the mucosa, however, does not occur at its most narrow part, but most frequently at about two-fifths of its length from the tip toward the base. The lumen of the body of the appendix varies greatly. Where it has been subject to high retention with subacute infection it enlarges gradually; where it has been subject to accumulating pressure with occlusion at the base without infection, it enlarges greatly to the size of the adult thumb or even larger. When the infection is severe the infiltration is great, and in these cases the subsequent cicatricial contraction diminishes the size of the lumen below its normal anatomical capacity, even to complete obliteration, when the epithelium is destroyed. These are the same pathological changes that take place in all of the hollow viscera under the same conditions, and particularly in the gall and urinary bladders.

The appendix has no vessel running parallel to its long axis; the vessels of the mesoappendix run directly through the mesentery to the appendical wall. At the mesenteric attachment there is no peritoneum. This is the weakest point in resistance under infection, and is the most common location of perforations where foreign bodies are present.

ETIOLOGY. When the disease was first recognized as a surgical affection, the acute infective lesions were considered to be due to the usual causes which produced enteritis in the remaining portion of the intestine and it was considered essentially a disease of the summer months. Now since we have become more familiar with it we find that it is almost as common in winter as in the summer. We find that it does not come on under the same climatic or dietary conditions as the other types of enteritis; that it most commonly follows exposures such as would produce so-called "cold" of the respiratory tract. So commonly is it a sequence of such exposure that a very prominent Chicago physician at one time considered it essentially a rheumatic manifestation. This, however, we do not accept.

Foreign bodies, as fruit seeds, gallstones, capsules, etc., were present in a little less than 2 per cent. of the cases. Fecal concretions were found in 38 per cent., and we believe that the erosion of the appendical mucosa by these foreign bodies produces an atrium for the admission of the infective flora into the tissue and precipitates under favorable conditions the acute attack. Indiscretions in diet appear to have little if any effect as an etiological factor.

The types of infective flora found in cultures and stainings from the appendices vary in the following order of frequency: bacillus coli communis, staphylococcus pyogenes aureus and albus, streptococcus, pneumococcus, bacillus tuberculosis, actinomycosis.

Appendicitis occurs in all classes with about equal frequency. In my work it has been a little more frequent in males than in females. I do not consider that it is contagious or infectious. It does seem, however, to have family predilections. This I would rather consider due to the conformation of the appendix or the diminished resistance to infection in some families and the comparative immunity to infection in others. I have not infrequently had two members of the same family in bed with the disease at the same time.

SYMPTOMATOLOGY. The symptoms in the order of their occurrence may be mentioned as: first, pain in the abdomen, sudden and severe, followed by (second) nausea or vomiting, even within a few hours, most commonly between three and four hours after the onset of pain; third, general abdominal sensitiveness most marked in the right side, or more particularly over the appendix; fourth, elevation of temperature, beginning from two to twenty-four hours after the onset of pain. In severe cases the temperature reaches 102° to 103° between eight and twelve hours after the initial pain. The symptoms occur almost without exception in the above order, and *when that order varies I always question the diagnosis.* If the nausea and vomiting or temperature precede the pain I feel certain that the case is not one of appendicitis. Where the

temperature alone precedes the pain for a day or even two or three, then I am always fearful that it is typhoid fever with a typhoid ulcer in the appendix. I have had seven cases of this class; the first three were operated and typhoid ulcers were found in the appendix; the last four were not operated; all went through classic typhoid courses after the appendical manifestations and all seven cases recovered. Where sensitiveness has been present for a number of days, and particularly where it is low in the pelvis, I have found the focus other than appendical—that is, due to infection of the tube, tuberculous peritonitis, etc.

Pain was a constant and uniform symptom and usually colicky in character, although patients varied in their expressions of its severity. In not a single case was it absent as an initial symptom. It usually reached its acme of intensity about four hours after its onset. It subsided gradually in the majority of cases. When it subsided suddenly, as it sometimes did, within the first thirty-six hours, the subsidence was due either to liberation of the infective material through the neck of the appendix into the caput coli, rupture of the appendical wall, or complete gangrene of the appendix. Under these conditions the pus pressure was relieved and the pus absorption diminished or stopped. With the cessation of pain in these cases, whether it was due to gangrene, intestinal escape or perforation, came the diminution or cessation of absorption, *but not* necessarily a *diminution* or *cessation of danger*, as is so commonly though erroneously interpreted, and often with fatal result.

The secondary pain, after the first thirty-six hours, is usually not colicky in character, but of the typical inflammatory type and due to periappendical involvements. Severe pain after the primary subsidence is always a signal of great danger, as it announces a beginning peritonitis from perforation.

The primary nausea and vomiting is reflex, due to overdistention of the appendix from the accumulating products of the infection, and is the same type of nausea and vomiting that we have with stone suddenly impacted in the neck of the bladder or suddenly passed into the ureter. There is usually only one or two efforts at emesis and the nausea then passes away. The secondary nausea and often persistent vomiting is due to the periappendical involvement; that is, infection of the peritoneum, and is of the same character and often the same persistence as vomiting from perforation of the tube, intestine, or stomach, into the peritoneum. In extensive peritoneal infections the vomiting continues to the fatal termination, increasing in frequency as time advances and as absorption increases.

The abdominal sensitiveness is first diffuse, although the abdominal wall is not particularly rigid. When the appendix becomes fully distended and tense it will not tolerate pressure and is pro-

tected by a marked rigidity of the abdominal muscles, the same as the gall-bladder and urinary bladder are protected under similar conditions when overdistended. As soon as the acute tension subsides, the general sensitiveness disappears. It becomes circumscribed to the area of the appendix, whether it be at McBurney's point, in the subhepatic space, or in the pelvis. When absent above, the pelvic examination should never be overlooked. If the sensitiveness has been once circumscribed to a small area and increases suddenly, preceded by pain and by secondary nausea and vomiting, it strongly indicates a perforation of the circumscribed adhesions and an infection of the general peritoneum. In endeavoring to palpate the appendix, after the first twenty-four hours, the greatest care and caution should be exercised. Severe pressure is likely to produce separation of friable adhesions that are of life-saving importance.

Temperature was not absent in a single acute infective case in its *early stage,* that is, in the first thirty-six hours after the onset of the symptoms. In the acute severe infections it is present in a few hours. In acute obstructions of the neck of the appendix, with mild infection, it appears later. In the calcular obstructions it does not appear until about the twentieth to the twenty-fourth hour after the beginning of pain. It is always present in the early stage of acute appendicitis. I would not operate on a case where I was confident that no temperature had been present in the first thirty-six hours of the disease. I came very close to making an unnecessary laparotomy in a case of this character. The patient had typical acute onset of pain, nausea, and vomiting, local sensitiveness and tumor; so sensitive was the tumor that manipulation was impossible. She was a doctor's daughter. Her father insisted that there had been no temperature at any time, but I felt that it was a case of the proverbial shoemaker's child, and that attention had not been close enough to warrant the statement that no temperature had been present. After she was on the table and I had taken up the scalpel, I laid it down again, saying that I had never had a case without elevation of temperature. With some manipulation the tumor disappeared under the costal arch and proved to be an acutely displaced kidney; no operation. When the patient recovered from the anæsthetic she informed us that in play at a picnic the second day previous she was rolled across the edge of a board fence, the pressure being from behind forward, just below the last rib. It caused her severe pain in her side and the pain continued from that time. This produced an acute displacement of the kidney with the symptoms of pain, reflex nausea, vomiting and extreme local sensitiveness, but with absence of temperature.

The temperature may all subside within twenty-four hours after the onset, and if it subsides suddenly I am fearful that the cause of its subsidence is a gangrene of the mucosa, with failure of further

absorption and therefore an intermission of temperature. Where it subsides gradually from thirty-six to fifty-two hours after the onset, then I believe it is due to a cessation of pressure from rupture of the appendix either into the mesoappendix or to circumscribed adhesions around the appendix. The temperature here, as in other places, must be recognized not as a manifestation of pus, but as a manifestation of absorption of the products of infection; without the absorption there is no elevation.

A remission of temperature of one or two or three degrees with subsequent gradual elevation means an infection of a new area of tissue. The temperature may go below 99° and remain there after the initial elevation, and still a large quantity of pus be present, either circumscribed or diffuse, in the peritoneum.

Secondary elevation of temperature should always be noted with apprehension, as it indicates a fresh invasion of tissue, a thrombophlebitis, a peritonitis, or cellular infiltration. These elevations are indications for immediate operation, and that usually means immediate drainage. Under these circumstances no extensive laceration of tissue or separation of adhesions should be attempted for the purpose of making a complete operation. The focus of pus should be drained and, as a rule, nothing more done

Leukocytosis. For a time it was believed that much valuable information could be obtained by ascertaining the excess of leukocytes. The more extended our experience, the less valuable it became. Leukocytosis may be considered a blood reaction to the absorption of septic products. Infection may be present without producing the blood reaction. A sudden and great increase in the number of leukocytes, supported by the other symptoms, is usually indicative of an extensive peritonitis.

Pulse. The character of the pulse has little value in the differential diagnosis of appendicitis. In children, when there is rapid absorption the pulse rate is very high. In the later stages of peritonitis, when it becomes compressible, rapid, and feeble, it is a fair index of the degree of intoxication and a guide to the prognosis rather than to the extent of the inflamed area.

In two cases of perforative appendicitis, where the perforation had occurred a number of hours before, the patients were walking around, with normal pulse and normal temperature. A considerable quantity of intestinal contents was free in the peritoneal cavity. One of these patients walked into the hospital with his doctor, did not appear materially sick, though the perforation had taken place eight hours before he presented himself. There had been some nausea and pain immediately after the perforation. That subsided and there was no change in his pulse or temperature. He was put on the table, the abdomen opened, and a large quantity of seropurulent material was found in the peritoneal cavity; also a con-

siderable quantity of fecal matter, which had leaked through a calcular perforation in the appendix.

Tumor. In the very early hours of appendicitis, while the inflammatory process is still confined within the appendix, an examination of the abdomen reveals an apparent tumor. The centre appears to be hard and fixed. It is oblong and about the size of the thumb. One feels convinced that the appendix rests close to the abdominal wall. The impression of tumor under these conditions is due to the spasmodic contraction of the muscle fibres directly over the situation of the appendix. When the patient is placed under the anæsthetic the tumor entirely disappears and, indeed, the appendix may be in the retrocæcal position and many inches from the abdominal wall. So frequent is this deception that I feel it should be constantly borne in mind. In the subacute cases the enlarged, swollen, and distended appendix can be frequently outlined by careful examination. As the periappendical tissues become involved and the quantity of infective material increases, the tumor becomes more pronounced and often attains considerable size. This is usually located in the right iliac fossa, but its absence from that position, with a clinical history indicating an appendicitis, must not be construed as meaning that the tumor is not present, because it will be found to be in the loin or low in the pelvis.

Fluctuation is only present when there is a large circumscribed abscess in the later stages of the disease. In the early stages of the disease the absence of peristalsis in the appendical region is of value in indicating the nature of the process. A careful examination with the stethoscope reveals a "still" area for many inches around the appendix.

The size of the tumor bears little relation to the quantity of pus. The area of infiltration around a streptococcus or staphylococcus infection is small, while the area of infiltration around the colon bacillus group of infections is always very large in proportion to the quantity of pus.

It is needless for me to go into details concerning the other minor corroborative signs of appendicitis, or to go into the many complications in the symptomatology of the later stages of the disease. The greatest difficulty is experienced in making a differential diagnosis between appendicitis and acute catarrhal conditions of the caput coli, or acute retention conditions in the caput coli, especially associated with the intestinal type of la grippe. Here we have the pain, nausea, and vomiting, the local sensitiveness and the elevation of temperature all combined, and so closely does it resemble appendicitis that in two cases I have erred in the diagnosis. In both there were evidences of previous attacks of appendicitis, with adhesions of the appendix, but in neither were there manifestations of an acute process in the appendix. Nor have my errors taught me a means of preventing their recurrence. I believe I

have avoided many errors in diagnosis by the stress which I placed on the order of symptoms as they occur, namely, pain, nausea and vomiting, local sensitiveness, and elevation of temperature; a deviation from this order causes me to seriously doubt the diagnosis of appendicitis.

Clinical Course. The clinical course of acute infective appendicitis is fairly uniform. In the acute infectious cases without calculus the mucosa becomes infiltrated and œdematous within an hour or two after inoculation. The œdema and infiltration increase rapidly and the compression of the inelastic coats of the appendix with the assistance of the biotic and toxic effects of the pathogenic flora produce a rapid gangrene of the mucosa, submucosa, and occasionally the entire thickness of the wall, with now and then complete gangrene of the appendix, so that a perforation of the appendical wall, on the average, takes place in from thirty-two to forty hours in virulent infections. Infection with the presence of a foreign body (fecal concretion) is usually associated with only a small area of gangrene, and that at the point of pressure of the calculus; here there is a local necrosis or gangrene with perforation and leakage; perforation in these cases takes place a little earlier than in the infections without a foreign body. Occasionally pressure ulceration and perforation of the appendix takes place at the seat of a coprolith without an acute infection. In this last class of cases the first announcement of the trouble is made by the initial symptoms of the perforation. These cases represent about 1 per cent. of all of the acute cases. It is a dangerous type for the patient, as the initial symptoms are attributed to a beginning appendicitis, when in reality they are due to a beginning perforative peritonitis.

In the streptococcus infections the mesoappendix and neighboring tissues are more seriously involved and the area of gangrene is less than with the colon bacillus or the staphylococcus types. The pain is most severe in the first six to fourteen hours; it becomes less as the necrosis advances; the temperature is highest from the sixteenth to the thirtieth hour, preceding the completion of the gangrenous process. If the gangrene continues to advance, the temperature remains up; if it becomes stationary, the temperature declines.

In one case of complete gangrene of the appendix the temperature was 104° nineteen hours after the onset of pain; it was 99.2° twenty-six hours after, at the time of operation. The appendix was gangrenous throughout its entire wall to its junction with the cæcum. It was a black, shining mass without an adhesion and slipped into the abdominal incision. The necrosis was so rapid and complete in this case that there was no effort on the wall of the appendix to fix itself to the neighboring tissues. I regard with alarm a sudden drop in the temperature and interpret it as meaning

a cessation of absorption, due, most commonly, to perforation of the wall of the appendix, with diminished pus pressure; second in frequency, to the escape of the contents of the appendix into the intestine; third, to gangrene of the wall; fourth, to circumscribing tissue infiltration with diminished absorption (local immunity); and, fifth, diminution of the virulence of the flora in accordance with the law of putrefaction and fermentation.

After fifty hours the clinical picture changes from that due to lesions of the appendix to that of infections of the periappendical regions. If the perforation takes place into the mesoappendix, or under circumscribing adhesions, the clinical presentations are those of a limited infection, while if the perforation takes place into the free peritoneal cavity the symptoms of a more or less severe peritonitis manifest themselves, depending upon the types of infection and the degree of involvement.

After a circumscribed abscess has formed, the temperature, pulse rate, and pain subside to a considerable degree; indeed, the temperature may approximate normal as the infiltration in the abscess wall becomes more and more pronounced and absorption proportionately diminished. If the rupture be into the postperitoneal cellular tissue, then there is rapid rise of temperature from the absorption. If the rupture be into the free peritoneal cavity, the rule is, first, a primary drop of temperature as the pus is relieved of pressure and the peritoneum has not yet been abraded of its endothelium, and therefore does not allow rapid absorption. In a staphylococcus infection of the milder type the peritoneum is first covered with an exudate, which may go on increasing in thickness to the formation of a membrane resembling the diphtheritic exudate. This exudate lessens the immediate absorption and protects the patient against an overdose of the septic products. It paralyzes peristalsis and produces coprostasis, but in a short time this plaque loosens, is thrown off, and carries with it the endothelial covering of the peritoneum, leaving a distinctly abraded or blistered surface from which there is rapid absorption and a sudden collapse of the patient, frequent bowel discharges, anxious expression, and shortly death. This sudden change in the staphylococcus infection of the peritoneum takes place between the evening of the fourth and the morning of the sixth day. If the primary infection of the appendix be of the streptococcus type and it ruptures into the peritoneum there is rapid blistering of the peritoneum and, within a few hours, symptoms of intense intoxication, high pulse, anxious expression, talkative delirium, quick perceptions, tympany, and all the manifestations of severe and acute streptococcus intoxication.

The action of the colon bacillus, when it gains entrance into the peritoneum, may be said to be midway between these two pictures. At times it produces but slight irritation, mild elevation

of temperature, considerable seropurulent exudate, and a gradually increasing disturbance of the surface of the endothelial covering of the peritoneum. The advancement is so slow that the tendency with this milder type is to circumscription of the process by peritoneal adhesions. On the other hand, under certain conditions, which we little understand, the colon bacillus may have a powerfully irritating effect on the peritoneum, produce rapid destruction of its lining cells, and expose its lymphatic stomata for rapid absorption. Indeed, its virulence may be so great as to produce gangrene of the peritoneum and even of the entire intestinal wall. This is fortunately rare, but is an extremely fatal type of the action of this bacillus. Sometimes the gas bacillus is associated with it and the tissue becomes emphysematous. There is not usually a high temperature in this class of cases, but great physical depression, lowered arterial tension, sunken eyes, somnolence, and finally low muttering delirium, differing entirely from the clinical picture of the streptococcus intoxication.

The quantity of pus found in the peritoneal cavity in the dry staphylococcus type is usually small. It may be large in quantity, and then it is of a seropurulent character. With the streptococcus type there is little, if any, free pus, but the peritoneum has that peculiar dry, granulating, blistered appearance which was so frequently seen in the post-partum sepsis of the pre-antiseptic period. The colon bacillus produces pus with an offensive odor, usually considerable in quantity and thick and creamy in character. The intestines are agglutinated together and many times separate pockets are formed. The elevation of temperature, the tympany, and the collapse are commonly slower in appearing with the colon bacillus than with either of the other types of infection. Collapse is not a sign of perforation, but a manifestation of the absorption of products of infection by an abraded or blistered peritoneum. It will appear rapidly or slowly after perforation, depending on the virulence of the infection and the rapidity with which the endothelium of the peritoneum is destroyed. This has been one of the most difficult lessons for the general profession to learn. For years we believed that collapse was an immediate manifestation of perforation; we must now recognize that it is a symptom of septic intoxication and always a late symptom, as far as the clinical course is concerned.

It can be seen from the various pathological conditions mentioned in the clinical course that a case of appendicitis may subside within a few hours by escape of the infective material along the tract of the appendix into the cæcum; that it may subside as a circumscribed inflammation of the appendix; that it may form a circumscribed infection without the production of pus in the free peritoneal cavity, with an inflammation only of the lymphatics of the mesoappendix and local peritoneum; that it may subside as a circumscribed

abscess outside the appendix, rupture through the wall of an adjacent coil of intestine, and empty itself in that way; that it may subside as a circumscribed peritoneal abscess and remain quiescent to be opened later; that it may terminate in a circumscribed or diffuse general suppurative peritonitis; that while it is a circumscribed abscess there may be a thrombophlebitis of the iliac veins, and the general venous circulation become infected with the manifestations of embolism, infarcts, and secondary abscess; that a portal venous branch may thrombose and hepatic abscess or pylephlebitis result; that there may be continuations of the infective process by contiguity of tissue or continuity of surface, extending down into the pelvis and up the opposite side of the abdomen, upward behind the peritoneum and around the kidney, upward beneath the surface of the liver and around the gall-bladder, or into the subphrenic space, through the diaphragm into the lung, and the pus be expelled through the mouth; or it may rupture into some portion of the urinary or genital tracts. All of these later and grave conditions are the sequences or the direct result of *omission* on the part of the surgical or medical attendants who had charge of the case during the first forty-eight hours of the appendicitis.

The closest attention has been paid in all of these cases to the relation between the symptoms and clinical course and the pathological findings, so that we may better anticipate the intra-abdominal changes by the symptoms and physical signs, or at least that we may know when and under what conditions pathological changes are not announced by appreciable symptoms, and thus avoid fatalities and surprises by a proper interpretation of the presence, order, or absence of symptoms.

I will not mention here the clinical course produced by the great variety of displacements, flexions, retentions, adhesions, torsions, and abnormal fixations of the appendix, as that would carry me beyond the scope of the paper. I must state, however, that we are just beginning to appreciate the great disturbance that can be produced in the intestinal tract and in the general metabolism, and the distressing and complex train of symptoms which result from these minor appendical lesions. We must operate much more frequently in the future for their relief than we have in the past, as we are learning from clinical experience that the disturbances produced by them are out of proportion to the logical deductions that could be made from the pathological conditions. The completeness of cures by operations on this class of cases is one of the most gratifying in the entire field of appendical surgery.

Time for Operative Intervention. The time for operative intervention may be divided into four stages: first, early, within the first forty-eight hours; second, in the active increasing inflammatory process, from the second to the fifth day; third, in the sub-

siding inflammatory process, from the fifth or seventh day on; and, fourth, in the intermediate stage—between attacks. From the previous statements concerning the clinical course and pathological changes, it can be seen that the most favorable time for operation is within the first forty-eight hours of the attack; or, from a pathological basis, before the perforation of the appendix or the infection of the periappendical tissue. The diagnosis can and should be made with accuracy in the great majority of cases before the end of the first twenty-four hours, and almost universally within the first forty-eight hours. From the symptoms and clinical course of the disease in the first forty-eight hours it is impossible to predict, with any degree of certainty, what the subsequent course of the case will be—that is, whether the tendency will be to subsidence and cure by natural processes or to a virulent, if not fatal, termination. This is the consensus of opinion of the large majority of those surgeons of greatest experience.

The danger of operative intervention in the early stage is scarcely more than that of an exploratory laparotomy. The time required for the convalescence is not more than two and a half to three weeks. Drainage is, as a rule, not indicated and hernia improbable. Unnecessary operations as a result of error in diagnosis would be very limited. The patient would, therefore, be relieved of his appendicitis without hazard, without prolonged illness, without the danger of unpleasant sequelæ, without the possibility of recurrence, by the only timely operation. To me there appears to be no excuse, no explanation, no logical process, no justifying hope that relieves the patient of the dangers of this disease. Procrastination, under these circumstances, I do not interpret as a manifestation of knowledge, experience, judgment, or true conservatism, but a stigma of their opposites. This should, therefore, be considered the period of election.

Should we operate in the second stage, during the increasing or spreading inflammatory process, which may mean anywhere from the second to the fifth day? In this stage we may have the circumscribed abscess around the appendix, the active inflammatory process of the neighboring tissues or organs, or the early pathological changes of a circumscribed or general peritonitis. We often find the temperature and pulse high, meteorismus, intestinal paralysis, and acute infected tissues, with manifestations of severe intoxication. These patients will not stand extensive manipulations. They are already fully burdened with the toxins, and this intoxication must not be increased or the patient will be sacrificed. Shall we operate? Yes, and in this stage. But the operation must be a limited one; that is, simple opening and relief of pus tension in the infected area with the removal of the appendix, if it be accessible and easily amputated. There should be the least possible separation of agglutinations or other trauma to the infected tissues. Agglu-

tinations and adhesions are life-saving, both in circumscribing the process and in rendering the local tissues unfit for absorption. Many of the fatalities in operations for appendicitis have been due to the failure of recognition of these facts. Where the patient is apparently overwhelmed with the intoxication from a circumscribed or diffuse peritonitis or inflammatory process, I content myself with making a simple incision in the abdomen and relieving the pus tension by the insertion of a large drainage tube without irrigation, without sponging, and without manipulation of the tissues. On the other hand, in the ascending stage of the disease, where the depression is not noticeable, when the intoxication is not severe, even when the quantity of pus is large, circumscribed or not circumscribed, the appendix is removed. In other words, the extent of operation is governed rather by the constitutional symptoms of the sepsis than by the extent or character of the pathological changes. One fact must never be lost sight of in operating on this class of cases, and that is, that the pus is usually virulent, and when organized adhesions are present they must not be separated, as they expose the surface to acute absorption. Organic adhesions are rarely formed before the fifth day. Exudates must not be rubbed nor torn off, as they carry with them the endothelia and leave an abraded absorbing surface. The peritoneum should be considered similar to the skin; in the latter, while the epithelia are intact, there is practically no absorption; they are the shingles of protection; with the peritoneum, while the endothelial cells are intact, there is practically no absorption. The rule, therefore, which I follow is not to treat any of the active inflammatory conditions on the expectant plan, but to relieve the suppurating infected centres by simply opening and inserting an efficient drain, and in the cases where the constitutional reaction is mild and the appendix accessible, it is removed. In my work the appendix has been removed in nine cases out of ten operated in the second stage, while if attempted in the 10 per cent. of selected cases, with severe symptoms of constitutional sepsis, the majority of them would be fatal. In the last two and a half years' work in general septic peritonitis I have had but one death following the operation, and that was a case of appendical origin, operated on the fifth day. The patient succumbed six days after the operation with a double pneumonia. The peritonitis had entirely subsided. This was the only death that occurred in any of the cases of peritonitis operated, including the typhoid, gastric, and intestinal perforations and sixteen consecutive cases of general suppurative peritonitis. The treatment after the operation in these cases consisted in placing the patients in a semisitting position, 35 to 45 degrees, retaining them in this position for three or four days, administering large quantities of saline solution (per rectum), from four to twelve quarts in twenty-four hours; the saline must be allowed to seep in, the tube remaining

constantly in position. No water was given by the mouth. The stomach never absorbs water, and under these conditions it does not readily transmit it to the intestines for absorption. Mild catharsis was induced with small doses of calomel, beginning eight hours after operation.

I am convinced that the great mortality which has been reported in operations in the second stage and under the clinical conditions mentioned above have, in a measure, been due to excessive manipulation, sponging, flushing, adhesion separating, and *prolonged operation.* The deaths in these cases of acute infection are due to the depression resulting from a sudden absorption of an overwhelming dose of toxin; this absorption is favored by the manipulations mentioned.

Let us contrast the treatment of an acute infective focus in the peritoneum with the treatment of a similar infection; for example, osteomyelitis in the ends of long bones. In the latter we open or tap without irrigation, sponging, curetting, or manipulation, and simply insert a drain. If we will treat the peritoneum with the same consideration we will have equally gratifying results. Water has no more license in the peritoneum than it has in the lung; the same may be said of trauma.

The posture after operation allows the pus to settle in the most dependent portion of the peritoneum; there it is pumped out through the tube by the alternating respiratory pressure. During transportation of cases of general suppurative peritonitis to the hospital the patients are kept in a sitting position; during operation they are kept in the same position. I do not consider any of these steps in the sense of life-saving stitches, but their combination and the results obtained have revolutionized my ideas and prognoses in general suppurative peritonitis, as well as in the acute and viciously septic appendicitis. Nor would I expect to cure a case of peritonitis in the stage of projectile, black vomitus; cold, clammy skin; pinched expression, ballooned abdomen, and dusky, cyanotic hue. Here, the fatal dose is already in the circulation, and inhibition, antitoxic eliminants, and hematodiluents would have no effect.

Operations in the third stage, or the stage of subsidence of the inflammatory process or retardation of the process of absorption, are not at all as urgent as in the first or second stage. To begin with, the destructive process has been overpowered by the local resistance of the tissue (the local immunity of tissue infiltration), and an effectual encapsulation has taken place; or they have been emptied through ulceration into a neighboring coil of intestine; or they are slowly destroying their boundaries in the line of least resistance and little absorption is taking place.

This process may continue for a considerable period of time unless some accident should rupture the wall, or the pus should come in contact with some vein and thrombophlebitis with embolism

ensue. The retained products of infection under these circumstances are always an element of danger, and in the hands of judicious and careful operators in this stage they can be conducted to the surface without hazard to the patient, and the appendix can, very frequently, be removed without extensive separation of adhesions or scattering the pus over non-infiltrated areas by carefully coffer-damming the operative field. If a mass is felt in the iliac fossa, pelvis, or loin, and is readily accessible in any of the positions, it should be opened directly over the most prominent point and drained. This, however, must always be the exceptional route. When a case has progressed to this stage, the patient is in a position to be placed in the best operative environment and to have the best skill. Personally, I open through the anterior abdominal wall in practically all of these cases and coffer-dam the field before opening the pus cavity. I have had six deaths in this class of cases, two in which the peritoneal cavity was not opened, but where the bulging abscess was simply opened and drained. In both of these the opening was made in the anterior abdominal wall without entering the free peritoneal cavity. Either from the preparatory manipulation or from pressure on the abscesses during operation they ruptured below into the free peritoneal cavity. Both were large abscesses, one in a fourteen-day and the other in an eleven-day case. The accident was not detected, as the pus flowed freely from the abscesses when they were incised. They died seventeen and twenty-six hours respectively after operation, from acute septic peritonitis. These cases occurred years ago, and since that time I never open directly into an abscess through an anterior incision. I always keep to the central side of the abscess and open into the free peritoneum, placing the coffer-dams before liberating the pus.

Three were operations in the third stage, with a secondary elevation of temperature and manifestations of absorption; two of these died from acute sapræmia from excessive separation of organized adhesions in efforts to remove the appendix in the presence of virulent pus. The other died from advancing gangrene with aërobic infection in which the intestines and local tissues sloughed. The sixth died of pylephlebitis with multiple hepatic abscesses. This I do not feel could be attributed to the operation, but to the fact that the operation was late and a thrombus had formed in the portal vein.

In the third stage the presence of pus is always an element of danger, and we should not feel content until it is removed.

In the fourth or intermediate stage the question arises, Should we operate on every patient who has been through an acute attack of appendicitis? If so, why? The reasons for operating that may be given are these: first, after an attack of appendicitis the patient is prone to recurrence; second, upward of 60 per cent. of the cases operated by me in the intermediate stage had had more than one

attack; third, in the large proportion of the cases in which there was only incision and drainage of the abscess (which was a procedure frequently recorded by me in my first three hundred cases) the attacks recurred. In one patient I drained a periappendical abscess on three different occasions, always with severe sepsis, before I succeeded in inducing the patient to come in between attacks to have the appendix removed; fourth, the pathological changes, such as adhesions, flexions, stenoses, etc., following a primary attack, very much favor a recurrence; fifth, even if there was no danger of recurrence of the inflammatory conditions, the adhesions, fixations, stenoses, flexions, and retentions in the appendix produce sufficient disturbance of the digestive tract to demand an operation for their prevention; sixth, recurrent infections are, practically, as dangerous as primary attacks (I recall one patient who died in the seventh attack); seventh, the appendix can be removed in the intermediate stage without danger. About two-thirds of the entire number of operations were in the so-called intermediate stage. In all of these I had one fatality and that was from an acute, infective peritonitis, traceable to an interne who had, without my knowledge, made a post-mortem on a post-abortion peritonitis the night before the operation; two other operations performed on the same day were similarly infected. I had one case of severe, but not fatal, hemorrhage, in the person of a physician, which was apparently due to penetration of the deep epigastric artery by the closing suture. This would mean about one death in 1300 or 1400 operations. In four of the intermediate cases only a stump of the appendix remained, as it was destroyed by the sloughing process. This is an extremely small number when one considers the severity of the inflammatory process and the number of cases in which the mucosa is gangrenous, as seen in the early operations. A partial or even complete obliteration of the lumen of the appendix is not rare.

The type of operation, as far as its application to many of the pathological conditions, has been mentioned from time to time in the progress of the paper. The routine incision is through the outer margin of the rectus, one-half inch to the central side of the linea semilunaris, rarely ever going through the transverse muscles or making the McArthur or McBurney incision. When the peritoneum is opened the finger is pressed down into the iliac muscles, drawn along the vessels upward until it hooks or lifts the ileum. This is followed out to the caput coli, the appendix located, freed, its mesentery compressed with heavy clamp forceps, and a catgut ligature placed in the crease. The mesentery is then divided, the base of the appendix is clamped with a heavy hæmostat, and a catgut ligature placed in the crease.

The appendix is then divided close to the ligature and embedded by two rows of fine linen sutures, always beginning on the meso-appendical line of the appendix; each row consists of three or four

continuous stitches; the stump is dropped. This is the procedure in the intermediate operation.

In the operations where infection is present, immediately after opening the abscess a coffer-dam, made of strips of gauze two and a half inches wide, is packed in on all sides of the infected area and retained there until the operation is completed. The abscess is then opened, the pus sponged out, the appendix located, if possible, and the adhesions gently liberated until a ligature can be placed upon the mesentery of the appendix. If the case be one of acute infection and virulent, as interpreted from the symptoms, a ligature is placed on the mesentery and one on the appendix, and both are amputated short, with no effort to embed the stump of the appendix. Notwithstanding the simplicity and this apparent imperfect closure of the appendix, I have not had a single case of fecal fistula requiring an operation for closure. In the septic peritonitis cases the appendix is always removed and a gauze and rubber drainage tube inserted, the latter going into the Douglas cul-de-sac or the vesico-rectal fold. A gauze drain alone in the presence of pus should never be relied on; the same is true of a cigarette drain. Where these are put in for the purpose of transmitting wound suction other than pus to the surface, they fulfil the intention for from eight to twenty hours after their insertion; then they become plugs, not drains. The most reliable and the safest drain is a rubber tube with small perforations. Portions of the coffer-dam around the field of operation may be permitted to remain for days after the operation. This is used less frequently now than it was years ago. The kind of drainage used is governed entirely by the character of the discharge. *All of the acute, severely infected cases are drained, even though the appendix has not perforated.* I consider that the area of the appendix and drainage makes me feel more secure. The drain, under these conditions, may be removed forty-eight to seventy-two hours after the operation. Dry sponges are always used and dry iodoform gauze coffer-dams. Irrigation is never resorted to in any of my abdominal work under any circumstances. The abdomen is closed with the layer sutures. A No. 2 dry catgut is used in the peritoneum, and so placed as to evert the cut edge of the peritoneum out into the abdominal wound and not expose it inside to form adhesions; a No. 4 is used in the aponeurosis of the rectus muscle and horse-hair for the skin. Occasionally a figure-of-8 silkworm-gut is used as an additional support in the aponeurosis of the rectus.

Immediately after the operation the patient is placed in a sitting position, 35 to 45 degrees, and kept there for from two to four days. This is not considered necessary in every case, but it is safer in most.

THE PATHOLOGICAL FINDINGS. It has been my endeavor to treat of the pathological findings in their relations to the symptoms or the stage of the disease, as well as the application of certain operative principles to definite pathological conditions. For a time it was my

practice to describe in detail what I expected to find in opening the abdomen, giving the pathological manifestations in detail. I must frankly confess that I have had many rude awakenings, although the average was fairly accurate. The errors, however, were so significant that had I changed from my rule of prompt action in every case, many lives would have been sacrificed. I was so impressed with these cases that the following expressions were used to the visiting physicians at the operating-table: "We do know from the clinical history, the symptoms, and physical signs that this is a case of appendicitis. We do not know what the tendency of the pathological process in this individual case is, whether it be toward security and repair or toward destruction and danger." A case in point: In a recent consultation, a surgeon of no small pretensions contended that the patient under consideration, then thirty-one hours after the onset of pain, whose pulse in the last six hours had fallen from 110 to 86, and whose temperature had fallen from 102.8° to 100.2°, was progressing favorably and operation might safely be postponed; but on the above rule it was insisted that no one could tell from these symptoms what pathological changes were taking place. The operation was accepted. The appendix was found free from adhesions, a circular gangrene one-half inch in length existed at about its middle, absorption had ceased, the line was clearly defined, and it is unnecessary to mention what would have been the result of delay. An early drop in temperature and pulse and cessation of pain cannot be relied upon as indication of a cessation of danger and must never be interpreted in that way. It only means a cessation of tension and absorption and not a subsidence of pathological changes or their subsequent dangers.

Subsequent Management of Cases. About 80 per cent. of the cases need very little, if any, special attention after the completion of the operation; 10 per cent. demand close watching and 10 per cent. the exercise of the greatest skill to conduct them to a favorable end, and it is to this last 10 per cent. that we will turn our attention. These are the ones that are already severely intoxicated, that have particularly septic processes, that have a local or general septic peritonitis. After the pus tension has been relieved by the opening and drainage and the source of the infection (the appendix) removed, the patient is placed in bed in the sitting (Fowler) position, with a back rest. This favors the settling of the peritoneal and wound exudates into the pelvis to the site of the drainage tube; it is a physiological fact that the pelvic peritoneum absorbs more slowly than the peritoneum above the umbilicus, and, furthermore, that encapsulation is favored by the anatomical structures in the pelvis and the activity of the omentum, sigmoid, and small intestines.

Then attention must be turned to elimination of the products

of infection. This is accomplished, first, by administering large quantities of fluids, rarely intravenous, occasionally subdermally, practically always per rectum and rarely by the stomach. Since we have learned that the stomach does not absorb water, and that in peritoneal inflammations and sepsis it does not readily force the water into the intestine for absorption, we have a good physiological basis for ceasing to give water by the stomach and good physiological explanation for the regurgitation of water administered by the stomach. We know from extensive clinical experience that very great quantities, one pint an hour, may be absorbed by the large intestine. The large quantity of water admitted into the circulation favors osmosis, dilutes the toxins, favors elimination, quiets thirst, lessens nausea, increases peristalsis and expulsion of gases. It is a matter of opinion through which of these channels we derive the greatest benefits. The stubborn fact remains, however, that the patient's comfort is greater, the condition improves, and they get well. Strychnine may have some value as supplementing the proctoclysis. If alcoholics are given at all they should be given by mouth, as they are rapidly absorbed by the stomach. Nuclein and unguentum Credé are beneficial in special cases, the former when the local resistance of the tissues seems to be meagre, the latter in the streptococcic types of infection with its exhilarative nerve phenomena. Calomel should be administered in small and repeated doses until effectual.

Immediate Results. The immediate results, if taken by hundreds, have varied very materially. The greatest mortality was in the first 100 cases, when it reached 11, and I might also add that in that 100 cases practically every one was an acute infection with pus perforation, more or less peritonitis, etc.; they embraced the cases from March 2, 1889, to July 23, 1893.

The number of deaths in each 100 then gradually decreased until after the meeting of the American Medical Association at Atlanta in May, 1896. It will be recalled that at that meeting there was a great cry against peritoneal operations and particularly against the frequent operations for appendicitis. This was heralded through the journals, and the general practitioner, believing it represented the consensus of opinion of the majority of surgeons, who were in close contact with the public, or general practitioners, accepted it as a fact and hesitated before advising operations when the unquestioned symptoms of appendicitis were present. The price in lives was great. The arguments urged represented the ideas of men who conducted large clinics, and not in close contact with the people or with the every-day practitioner, who saw mostly intermediate cases and did not realize the virulence, rapidity of destruction and danger, as well as the consequent vital importance of prompt and early action in the acute infective stage. In the year following this meeting the mortality reached 7 in 100. Then

there was another gradual decline, as the error of the position was recognized, until a second epidemic of so-called conservatism ("expectant treatment") passed over the country and carried with it its quota of deaths, when the mortality reached 6 in 100. For the last four years there has been a steady decline in the number until in the last 100 operations there was a mortality of 2 per cent. One of these deaths was due to an ileus of the small intestine high up, bearing no relation either in adhesions or otherwise to the appendical operation, and the other a death from a double pneumonia six days after the operation for general septic peritonitis of appendical origin, the peritonitis having entirely subsided.

It seems to me that every death from appendicitis is chargeable directly to the people, either for not calling in the physician sufficiently early after the onset of symptoms, or to the physician and surgeon for not acting promptly when they are called. I am sorry to admit that the latter represents the greater percentage. We should have no deaths from appendicitis, but *we are having them.* We should accept the force of numbers and experience to guide us against the culpable if not criminal error of delay in this class of cases. It is not necessary that every physician should lose a case so he may learn the lesson, any more than a doctor should lose a case under chloroform anæsthesia before he learns either to abandon it or have it administered by competent hands.

Final Results. The final results in appendicitis, as a whole, are very gratifying. When a patient has had the appendix removed, the rule is that he recovers from the operation, has as good if not better health than he had before, and is free from pain and inconvenience in the right hypochondriac region or disturbance of his digestive tract as a result of the disease or the operation. It is surprising how completely extensive adhesions, the result of diffuse and extensive inflammatory processes, disappear soon after the focus of infection is removed and the source of irritation eradicated. Prolonged packing and drainage tend to the formation of more firm adhesions than usually result from the inflammatory processes with their adhesions in limiting the infective process. With the exception of the adhesions following tuberculosis in the peritoneum, there is no other lesion in which the adhesions so rapidly and completely disappear as those that exist around an inflamed appendix. If the appendix has perforated and a secondary perforation has taken place into the intestine, a firm and organic adhesion of the appendix may remain, uniting it to the intestine, the caput coli, or the ileum, as the case may be. It seems to me even these rapidly absorb, so that in an abdomen where six weeks previous an operation had been performed for the drainage of a large periappendical abscess, with extensive suppuration and adhesions, almost every evidence of the disease, except a fluffy, velvety condition of the peritoneum, had disappeared. This is an every-day observation.

The regenerative power of the epithelium over the intestine is vast in the average case. Occasionally we find a tendency to keloid formations in the peritoneum, or to the formation of cord-like adhesions which develop into strong, firm bands of sufficient power to lift the patient from the table. Fortunately these are rare. If the appendix remains and becomes a chronic source of irritation after an attack of appendicitis, the adhesions often continue and remain there as a protection against a subsequent attack, rendering the danger in a subsequent attack less in these cases. If we could only tell from the symptoms that they existed, what a comfort it would be in recurrences!

Hernia. Much has been written on the subject of hernia following the operation for appendicitis, and many suggestions have been made concerning the original incision. It seems that one of two incisions should be adopted: either the gridiron incision of McBurney and McArthur, or the incision through the rectus muscle. The gridiron incision has the advantage of retaining the muscle fibres without injury while it divides the muscular sheath, which is often strong, at the point of separation of the fibres. It has the disadvantage of confining the operator to a comparatively small field after the abdomen is opened, unless he is willing to sacrifice the muscle by division. This is not such a serious matter as we formerly believed. Muscle fibres may be divided in a direct transverse line if they are again brought into apposition and the full strength of the muscle retained. This is seen in division of the biceps, triceps, and the abdominal rectus. It leaves a depression and a deformity, but no deficiency in support. The other incision is one to the central side of the linea semilunaris, going through the rectus muscle. It has the advantage of permitting the incision to be elongated from the symphysis to the costal arch without the division of muscle fibres. It has the further advantage of permitting the peritoneal and the muscular aponeurosis to be sutured without including the muscle fibres and, at the same time, produces approximation of the slit muscular fibres side to side in their long axis, the sutures being applied in layers. The accurate apposition of the aponeurosis of the rectus with a catgut or figure-of-8 suture practically guarantees against a hernia. In the class of cases in which drainage is necessary there is a defect in the approximation of the aponeurosis of the rectus or of the muscle fibres if the gridiron incision be made, which leaves a weakness in the wall; this, in a considerable percentage of cases, results in hernia. Prolonged drainage is not so frequently necessary as was formerly supposed. A figure-of-8 suture, to be tied later, can be used for the approximation of the cut edges of the aponeurosis at this point. It should be allowed to remain loose until the drainage is removed, and then it may be drawn taut and good apposition secured, which will lessen the likelihood of hernia, though it will not prevent an

occasional one. If the postoperative hernia is tending to increase, it should be closed with an edge-to-edge union of the aponeurosis, or a flap operation of the aponeurosis, after the method of Mayo for umbilical hernia. Hernia bears close relation to drainage in all locations of incision in the abdominal wall.

Obligations of the General Practitioner. My early experience with appendicitis occurred when I was doing general practice, the first operation having been performed at Cook County Hospital on March 2, 1889, which I believe was the first one in this country under the new idea of the surgical treatment of appendical and perityphlitic affections or induration—*i. e.*, operating in the absence of phlegmon, but on the theory that the primary lesion was an infection and suppuration in the appendix and the perityphlitis, a secondary extension of this infection. Periappendical abscesses with phlegmon and induration had been drained and earlier intervention urged in most forceful language by Bull and others preceding that time. (The report of this operation was made to the Chicago Medical Society, November 4, 1889.) This operation was performed after reading the able paper of Krufft, which I think did more to stimulate early operations on the appendix at that time than any other paper that appeared. Therefore, I make no apology for speaking of the obligations of the general practitioner in appendicitis. In a large number of the early cases of appendicitis I was the first doctor called, and after a few experiences, which were so forceful in their instruction, it required no courage on my part to insist on the operation. Many of the first hundred operations were performed on the kitchen-table, with the ordinary aseptic conditions that could be secured in a twenty-minute or half-hour preparation. In a large number of them there was no trained nurse, no cumbersome excessive surgical paraphernalia, avoiding the loss of time which these entailed, hastening the liberation of the pus or the removal of the appendix, as the case might be. The facts gleaned at that time made me realize, as no subsequent experience has, the degree of destruction that can occur in a very limited number of hours with virulent infection of the appendix. Indeed, I was frequently asked, "Where do you get all of the appendicitis cases?" with a look and an inflection that did not indicate the utmost confidence in my diagnostic ability or the integrity of the numerals; but that is ancient history. Appendicitis has come and it has come to stay, and the responsibility of its immediate recognition is on the general practitioner. It seems to me that a man has no more right to hope that an inflammation of the appendix, once instituted, will tend to a favorable termination than he has to hope that an acute, infective osteomyelitis of the femur, or a phlegmon of the thigh, will recover without liberation of the pus.

Can the general practitioner make an early and accurate diagnosis? Yes. This is admitted by all at the present time. Is he

justified in hoping that the case will subside and go through to a favorable termination? No! We will admit that 80 per cent. of the cases recover from the attack; that 20 per cent., approximately, of the cases either die in the first attack or have recurrences. If he decides to wait, it is with the understanding that he is willing to sacrifice that percentage of his patients. All aid can as readily be timely as untimely. It seems to me that as a general practitioner I would feel personally responsible for the death of a patient suffering from a typical attack of acute appendicitis, if I had the case from the beginning and was called early—that is, in the primary pain. I might endeavor to ease my conscience by urging certain reasons for withholding action, or by stating that I was following Smith's or Brown's or Jones' plan of treatment, but the ever-living witness of inner judgment would be crying out against me. There is no plan of treatment which controls the pathological processes. There is no plan of medical treatment which materially lessens the risk. There is no system of beating the mortality percentages in appendicitis.

I wish to express my high appreciation of the strong position taken by many of the ablest medical men in insisting that they have no power of control over the disease, and that it is essentially from its initiation a surgical condition. Indeed, these men outrank many of the surgeons in their judgment and in their appreciation of the urgency of immediate action.

Obligations of the Surgeon. The obligation of the surgeon is to conduct a case of appendicitis to a favorable termination *with the least hazard or risk to the patient*, regardless of his personal or professional feeling or of the praise or condemnation of his conduct. We all meet cases where we would readily shirk the responsibility of action, but we have no license in the role of surgeons if we take that position. We all meet cases in which we would prefer to have one clean operation and be through with the case, but that must never be done where it involves additional hazard to the patient. A second operation with a living patient at the end is better than a primary radical operation with a mortality of two or three in a hundred as the price. This involves the element of individual judgment and cannot be adequately described. The man who is having more than three or four deaths in a hundred operations for appendicitis is either receiving his patronage from incompetent and procrastinating medical men, or he is doing too much manipulating in the peritoneal cavity under unfavorable pathological conditions. There are practitioners who recognize the earliest symptoms, and, indeed, I recall one who forced me on two occasions to operate where I was not satisfied of the diagnosis, and on each occasion he was correct.

The transportation of patients after the onset of an attack of appendicitis is an important factor, and one that comes under the

class of surgeon's obligations. If the case is brought to my attention before the thirtieth hour I feel that the patient can be transported to the hospital with safety. If, on the other hand, it is after that time it is safer to have the operation performed in the environment of his home, whatever that home may mean. If the patients are to be transported, they should be kept in the sitting position on the stretcher. Once the surgeon has operated he is obligated for all of the details of the case to a complete convalescence. If the associate is sufficiently competent to care for the patient under his instruction, well and good; otherwise he must see to it himself that all of the details are carried out to a complete and perfect convalescence.

PSEUDOMELANOSIS OF THE HÆMOLYMPH GLANDS.

By Aldred Scott Warthin, Ph.D., M.D.,
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The writer's contention that lymphoid structures containing sinuses filled with red blood cells and showing evidences of extensive phagocytic hæmolysis are constantly present in the human retroperitoneal tissues has been widely accepted during the last two years. His statement that the hæmolytic activity of these organs is relatively greater than that of the spleen has been recently confirmed by Lewis,[1] who made comparative counts of the number of phagocytes containing red cells and pigment occurring in equal fields of the spleen and hæmolymph nodes. A number of organs were cut and several sections from each examined. In each section as many isolated fields as possible were taken with a $\frac{1}{6}$ objective, and the number of phagocytes containing red cells or pigment particles in each field were counted. Estimates were also made of the number of red cells enclosed within the phagocytes. From the results of these observations a few examples may be taken: In the case of the rat the proportion of phagocytes in the spleen was 1.6 to 93 approximately in the hæmolymph nodes; in the rabbit 1.2 in the spleen to 60 in the hæmolymph nodes; in the sheep 0.5 in the spleen to 31 in the hæmolymph nodes. In all cases the hæmolymph nodes showed by far the greatest amount of phagocytosis per average field.

Similar results have been obtained by the writer, and the suggestion made by him in 1902 that these nodes might properly be styled "hæmolytic glands" acquires additional force. Further confirmation of the marked hæmolytic activity occurring in these glands is shown by the striking and very interesting findings in the

[1] Journal of Anatomy and Physiology, vol. xxxviii.

following three cases occurring in the autopsy service of the University Hospital.

CASE I.—Miss K. C., aged twenty-six years. Right tube and ovary removed by vaginal route; operation followed by diphtheritic vaginitis, gangrene of the vaginal wound, and general fibrinous peritonitis. Autopsy five hours after death: abdomen slightly distended; small patches of dark-gray to greenish-gray discoloration over the abdomen and the upper parts of the thighs; at these areas of discoloration there is a well-marked subcutaneous emphysema. (Both the discoloration and emphysema were present before death, but increased to some extent during the five hours between that event and the autopsy.) On opening the body a strong odor of H_2S was perceptible, particularly in the abdominal cavity. Gas-bubbles were present in the blood of the large veins and heart. The cut surface of the lungs gave a strong odor of H_2S. No discoloration of the thoracic organs. The peritoneal exudate and the intestines presented no discoloration. Red blood clots were found in the pelvis. The spleen was bluish red, and showed no trace of pseudomelanotic discoloration. The edges of the vaginal wound were blackened and friable. Section of the dark patches in the subcutaneous tissue of the abdominal wall and thighs showed blackened areas containing gas-bubbles, but no macroscopic evidences of tissue disintegration. The odor of H_2S was distinctly perceptible immediately upon cutting into these patches, but was soon lost.

Hæmolymph Nodes. On exposing the retroperitoneal region there were visible in the prevertebral tissues, at the sides and behind the great vessels, about forty-five grayish to black glands occupying the usual site of the hæmolymph glands. The tissues about the dark glands showed no trace of discoloration, so that the latter stood out in sharp contrast to the light color of the former. Whitish and pinkish glands were found side by side with the dark ones. The majority of the discolored nodes were oval or bean-shaped, or flattened. They varied in length from 1 to 3 cm. and in diameter 0.5 to 1 cm. On section the dark discoloration of some appeared uniform throughout the gland; in others the discoloration was most marked in stripes and spots corresponding to the sinuses. The entire retroperitoneal tissues were dissected out and put into the first Kaiserling solution (formaldehyde, 200 c.c.; water, 1000 c.c.; potassium nitrate, 15 grams; potassium acetate, 30 grams). In twelve hours the dark color had become replaced by a light grayish, and after running the tissue through the three solutions all trace of discoloration had disappeared and the glands had become of a brownish-red color.

The microscopic examination of some of the dark glands fixed in mercuric chloride showed them to be hæmolymph nodes showing an increased number of phagocytes containing a brownish, granular

pigment which responded to the iron test with potassium ferrocyanide and HCl acid. No bacteria were seen in the pigmented glands. Sections of the edges of the vaginal wound showed an organizing fibrinous exudate containing blood-pigment and numerous colonies of bacilli. No sections were made of the dark areas in the subcutaneous tissues of the thigh.

The bacteriological examination resulted in the obtaining of pure cultures of colon bacilli from the heart blood and the peritoneal exudate.

Case II.—Mr. G. H., aged forty-two years. Transverse myelitis (fracture of fourth and fifth cervical vertebræ); decubitus; chronic cystitis and pyelonephritis; chronic purulent bronchitis and bronchiectasis; general marasmus. Autopsy eleven hours after death: abdomen on level of ribs; large bed-sore on sacrum, having edges gray to black in color; small amount of clear fluid in peritoneal cavity; no peritonitis; no odor of H_2S in either thorax or abdomen; no discoloration of spleen, intestines, or other abdominal organs. On removing the intestines and mesentery and exposing the retroperitoneal tissues, an exactly similar picture to that seen in Case I. was found. Along and behind the abdominal aorta and vena cava were forty to forty-five dark-gray to black glands standing out distinctly in the light fat and connective tissues. Glands of pale and pink color were found side by side with the dark ones. The right psoas was pale and soft; the left one was very soft and of the same color as the dark glands. No odor of H_2S could be perceived.

An attempt was again made to make a gross museum specimen of the retroperitoneal tissues by the Kaiserling method, with the same results as in the first case. The dark-gray or black color quickly disappeared from the glands, and in alcohol the latter became red or brownish red.

The microscopic examination showed the dark glands to be hæmolymph glands containing an increased number of pigmented phagocytes. With potassium ferrocyanide and HCl acid the greater part of the pigment gave the iron reaction. No bacteria were found in the glands. In the liver the cells of the central portions of the lobules contained a large amount of a yellowish-brown pigment which did not give the iron reaction. Numerous phagocytes containing iron were found in the spleen.

The bacteriological examination of material taken from the bed-sores yielded five saprophytic organisms not fully identified. Staphylococcus aureus was obtained from the bronchial pus.

Case III.—Mrs. R. Operation for removal of ovarian carcinoma followed by abscess of abdominal wall and beginning peritonitis; patient died suddenly of acute cardiac dilatation. Autopsy three hours after death; strong odor of H_2S in peritoneal cavity and in abscess of abdominal wall; no discoloration of peritoneum, peritoneal exudate, or of abdominal organs; wall of abscess gray-

ish; no odor of H_2S perceived in lungs or heart; retroperitoneal hæmolymph nodes enlarged, apparently hyperplastic, about forty in number, and of a dark-gray color, standing out very prominently in the light adipose tissue; pink and whitish glands were found in association with the discolored ones; no odor of H_2S in retroperitoneal tissues. The prevertebral tissues were dissected out and put into the first Kaiserling solution, in which the gray color gradually changed to a brown, becoming reddish when put into alcohol.

The microscopic examination of the hæmolymph nodes showed them to be hyperplastic, the sinuses filled with phagocytes containing blood pigment. Numerous hyaline areas staining red with acid fuchsin were found throughout the lymphoid tissue of the nodes. With potassium ferrocyanide and HCl the iron reaction was obtained with the greater part of the pigment in the phagocytes, and fine granules of hæmosiderin were also found in the hyaline areas. No hæmosiderin was found in the liver, but it was present in large amount in the spleen.

The bacteriological examination resulted in the isolation of a bacillus belonging to the colon group from the pus of the abscess in the abdominal wall and from the peritoneal exudate. No other organism found.

Summary. The striking feature possessed in common by these three cases is the grayish or black discoloration of the retroperitoneal hæmolymph nodes in the absence of any similar discoloration of the spleen or other abdominal organs. The occurrence of such discoloration can hardly be explained otherwise than as due to a combination of H_2S and the iron-containing blood pigment found in the phagocytes present in the sinuses of the affected nodes. As to the source of the H_2S, it is evident in all three cases that the gas was formed, not in the intestinal canal, but in local infected foci or in the blood. In the first case there was a general colon bacillus infection arising from the infected seat of operation in the vagina and pelvis. Throughout the entire body there was a strong odor of H_2S. In the second case there was a saprophytic infection of the bed-sore, with secondary involvement of the left psoas. Though no odor of H_2S could be perceived in this case, there can hardly be any doubt that the discoloration was due to its presence. In the third case there was a strong odor of the gas in the peritoneal cavity and abdominal abscess, and from these regions a bacillus belonging to the colon group was isolated. Each case therefore presents an adequate source of origin for the gas and a definite cause for its formation, and in two of the cases its presence was evident through the strong odor.

It is probable (certain in one case) that the formation of H_2S began before death, and that the appearances presented by the hæmolymph nodes were not wholly the result of post-mortem changes and conditions. It is of minor importance, however,

whether the gas was formed before or after death. The important point is the fact that in the hæmolymph nodes there may be such a quantity of iron-containing pigment that these nodes may take up H_2S and become grayish or black in color, while the spleen remains unchanged in appearance.

Such a phenomenon may be explained by the fact that the gas does not gain entrance into the spleen pulp as readily as into the hæmolymph nodes, or that the amount of iron-containing blood pigment is greater in these nodes than in the spleen, or that the iron-containing pigment in the hæmolymph nodes combines more readily with H_2S than does that in the spleen. On comparing sections of spleen and hæmolymph nodes tested for iron with potassium ferrocyanide and HCl acid, the amount of iron-containing pigment in the hæmolymph nodes is relatively much greater than in the spleen. Nevertheless, in two of the cases numerous phagocytes containing iron were present in the spleen, although this organ at autopsy showed no trace of discoloration. The other two factors must therefore be considered as possible.

That the combination of the H_2S with the iron pigment is very loose is shown by the rapid disappearance of the black discoloration in all the usual fixing fluids. A similar change took place more slowly on simple exposure to the air. In the case of the Kaiserling method the black color was replaced by the normal red or reddish-brown color of the hæmolymph nodes. The gas is therefore probably given off very readily from its combination with the iron pigment.

The combination of H_2S with the iron-containing blood pigment of the nodes seems to be a satisfactory explanation for the pseudomelanosis in these three cases. The theory advanced by Borst,[1] that the discoloration of pseudomelanosis may in some cases be due to a reduction of iron pigment to metallic iron, receives no support in the findings of these cases. The view of Ernst,[2] that local pseudomelanosis is due to a local growth of hydrogen-sulphide-forming bacteria, applies in part to these cases. The discoloration of the edge of the vaginal wound and the black patches containing gas in the skin of Case I., the discoloration of the bed-sore and psoas muscle in Case II., and the discoloration of the abscess wall in Case III. were undoubtedly due to the local growth of bacteria producing H_2S and the combination of the gas with blood-pigment resulting from local extravasations. It is doubtful, however, if such an explanation will hold good for the origin of the pseudomelanosis of the hæmolymph nodes, inasmuch as no bacteria could be demonstrated microscopically in these. In the first case there was most probably a colon bacteriæmia, the bacillus being obtained in a pure culture from the heart's blood; so that it is prob-

[1] Virchow's Archiv, Bd. cxlvii.

[2] Ibid., Bd. clii.

able that colon bacilli were present, to some extent at least, in the sinuses of the hæmolymph nodes. Taking everything into consideration, it seems most probable that the pseudomelanosis of the hæmolymph nodes in all three cases was due to an absorption of H_2S from the blood or through the tissues rather than to a local formation of gas in the sinuses of these organs.

Such a localization of pseudomelanosis as described above has not, to my knowledge, been previously recorded. This is, however, not of so great importance as the strong additional proof offered of the marked hæmolytic activity of the hæmolymph nodes.

NOTE.—The exposure to H_2S of hæmolymph nodes obtained from cattle and sheep produced results exactly like the findings in the above cases. The nodes quickly became discolored; some becoming uniformly grayish black or brownish black, others becoming spotted or streaked. The discoloration thus produced lasted for a longer time than that seen in the autopsy cases.

A STUDY OF THE TUBERCLE BACILLI ISOLATED FROM THREE CASES OF TUBERCULOSIS OF THE MESENTERIC LYMPH NODES.[1]

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THE desirability of studying tubercle bacilli from those cases of tuberculosis which are presumably the result of food infection was emphasized by me[2] in 1898 as the surest way of gaining an insight into the relation between bovine and human tuberculosis. In a more recent contribution[3] I described among other cultures two from the mesenteric glands of children, one of which (Human XI.) was pronounced to be of bovine origin. At the same time I supplemented the studies made by Ravenel upon a presumably bovine culture (BB) from a child by applying a new reaction test there described for the first time. This latter culture had also the characteristics belonging to the bovine bacillus.

I shall not attempt to review certain articles which have appeared since the conclusion of the manuscript of my former communication in May, 1903, since they do not bear directly upon the contents of this paper, but simply begin with the statement that no observations have thus far been presented which invalidate the distinction between

[1] Read before the Association of American Physicians, May, 1904.
[2] Journal of Experimental Medicine, 1898, vol. iii. p. 451.
[3] Transactions of the Association of American Physicians, 1903, vol. xviii. pp. 109–151.

the bovine and the human race or variety of tubercle bacilli made by me in 1898. This distinction, as I then clearly stated, does not imply that the bovine bacilli, under certain conditions, might not invade the human subject.

In the following pages three cultures, all of them from the mesenteric lymph nodes of human beings, are studied from those points of view best adapted to inform us whether they are of the bovine or of the human variety

Human Culture XIII.

For the material from which this culture was isolated I am indebted to Prof. Mallory and to Dr. H. A. Christian, who performed the autopsy, from the protocol of which extracts are given below.

The case was that of an infant, eight months old, in the service of Dr. T. M. Rotch, at the Children's Hospital, Boston, Massachusetts. The clinical history may be very briefly summarized:

About three months before admission the child began to have swelling of glands on the left side of neck and face. These have been opened, but they have recurred again and again. There has been coryza for two months, which has interfered with nursing. The lesion of the neck was incised, the pus pressed out and proper treatment instituted. There was no positive reaction from two injections of tuberculin given on the seventh and the ninth days. The child died on the fourteenth day after admission. The autopsy, performed fifty-four hours post-mortem, brought out the following pathological conditions:

"There was pneumonia in both lungs, but no evidence of tuberculosis in any of the organs of the thorax.

"In the abdomen the mesenteric lymph nodes are enlarged, and many of them soft and cheesy. In the spleen there are miliary tubercles.

"In the ileum, close to the ileocæcal valve, there is a small yellowish nodule which projects slightly into the lumen of the intestine. The mucous membrane over this is intact, and the size of the nodule does not exceed 4 mm. In the ascending colon there is a somewhat similar lesion a little larger and over the surface of which the mucosa is slightly ulcerated and somewhat pigmented. With the exception of these two lesions the intestinal tract was normal.

"Liver, weight 310 grams. The surface is a pale tawny pink, and scattered over it are numerous nodules, from 3 to 5 mm. in diameter, which are lighter in color. Some of these project considerably above the surface of the liver, others project but slightly. Just at the periphery of each there is a slight depression in the liver, giving the areas a somewhat button-like appearance. On the cut surface these nodules are yellowish or grayish in color, and many of them can be made out to be formed of smaller coalesced areas of similar character. On the surface of the liver some similar

nodules are seen always near the surface, and, as a rule, extending to the surface of the liver. In the tissue about some of the bloodvessels a few small grayish points, probably miliary tubercles, can be made out.

"Throughout the meninges can be seen a few generally widely separated and very small, grayish areas. In a few places these become much more numerous and more closely set. This is particularly true of the adjacent surface of the posterior portion of the longitudinal fissure and the superior median surface of the cerebellum. This is also true of the surface of the island of Reil, in which, on both sides, there is a conglomerate tubercle fully 1 cm. in diameter, firm, of a yellowish color, and closely adherent to the surface of the cortex, though apparently not embedded in it. Over the base of the brain, particularly along the surface of the medulla, pons, and basal ganglia, there is a moderate amount of yellowish fibrinous exudate. This is also present over the anterior portions of the temporal lobes, and here appears to have a more purulent character."

The anatomical diagnosis includes tuberculous, exudative, and miliary meningitis, conglomerate tubercle in the island of Reil on both sides, tuberculous nodules in intestine, caseous tuberculosis of mesenteric lymph nodes, conglomerate tuberculosis of liver, and miliary tuberculosis of spleen.

The culture was obtained from one of the mesenteric lymph nodes. These were about 1 cm. in diameter, centrally soft, caseous. In several smears tubercle bacilli were not found. A dense suspension of caseous material in normal salt solution was injected into the abdomen of three guinea-pigs. Cultures were obtained on dog serum, horse serum, or egg medium from all of the guinea-pigs. The growth and appearance in all the tubes indicated identity. In all cases the development was prompt and vigorous, indicative of the human race bacilli. The growths became heavy, coalescing, smooth or wrinkled membranes. In some cases well-isolated, smooth, roundish colonies were obtained. Good growth on glycerin agar followed the inoculation of subcultures. In the earliest cultures the bacilli appeared as solid rods, of somewhat variable length, measuring from 1 to 2.2μ in length. In somewhat later cultures they were so irregular and polymorphic in outline that measurement was impossible. The preliminary inoculation of guinea-pigs with tissue had already indicated bacilli of a low degree of virulence. The subsequent tests upon rabbits and guinea-pigs with definite suspensions of pure cultures confirmed the early inference. In Table I. the result of tests upon rabbits, in Table II. those on guinea-pigs are given. In both species marked resistance to this bacillus is manifest.

That it is not an attenuated or modified bovine culture is made evident by the culture reactions given in Table III. For the sake of

comparison a bovine culture was included in each group of cultures. In all three tests the difference between the bovine and the human races is in evidence.

Human Culture XIV.

This bacillus was isolated from material obtained through professor Mallory. The patient, a Chinaman, aged twenty-six years, was admitted to the Boston City Hospital suffering from nausea and pain in the stomach. Physical examination revealed nothing unusual.

During his stay in the hospital the temperature fluctuated between normal and 104° F. Rales developed in both lungs, which gradually increased in intensity, although no definite consolidation could be detected. The patient died on the sixteenth day after admission, after a gradual failure of heart and respiration. From the autopsy protocol of Dr. Mallory the following points are of interest to us:

In the peritoneal cavity "surfaces smooth and shiny, with no increase in fluids. Mesenteric lymph nodes much enlarged. One of the glands measured 2 cm. diameter; glands were confluent. On section there was revealed a yellowish, cream-cheese-like substance; a smear from the same reveals B. tuberculosis.

"*Pleural Cavity.* Left lung bound everywhere by rather strong fibrous adhesions. On separating the costal and parietal pleura many minute, grayish, raised areas are seen.

"*Lungs.* Dark-red, hubbly surface, non-crepitant throughout, except for a few subcrepitant areas at the apices. On section surface is dark red, rather dry, and scattered everywhere are grayish-white areas, averaging 2 to 3 mm. in diameter, discrete, often confluent. Bronchial lymph nodes not enlarged. Bronchi filled with mucopurulent material.

"*Kidneys.* Scattered throughout cortex and in pyramidal region are a number of yellowish-gray areas not raised above the surface, averaging 2 mm. diamater, discrete for most part, occasionally confluent."

The anatomical diagnosis included miliary tuberculosis of the lungs and kidneys, tuberculosis of the mesenteric lymph nodes, and acute tubercular pleuritis. In this case the evidence obtained from the post-mortem examination suggested primary tuberculosis of the mesenteric glands which furnished the infection for the fatal miliary tuberculosis.

The source of the culture studied was a mesenteric lymph node about as large as a horse-chestnut. It was almost wholly converted into a soft caseous mass. In several smears bacilli were not detected. The isolation was made as in the preceding case, by injecting a suspension of the cheesy matter into the peritoneal cavity of

three guinea-pigs. The disease in the guinea-pigs was so slight that they all greatly increased in weight during the six weeks following the inoculation. In one, chloroformed after ten weeks, no lesions could be found and no cultures were attempted. In the remaining two the lesions were characteristic, though slight, and nearly all cultures made developed rich crops of colonies, isolated and confluent. Only the cultures from one guinea-pig were tested on animals and in bouillon cultures for the reaction curve.

The bacilli were slightly curved rods, 1.5 to 2.5μ long, the greater number being about 2μ in length. Cultivation on glycerin agar, glycerinized potato, and horse serum yielded cultures quite vigorous, although they did not equal in richness those on dog serum.

One rabbit (Table I.) which received twice the standard dose was chloroformed after one month because suffering with snuffles or rhinitis. The lesions found were very slight. The second rabbit, which received the usual dose, was also affected very slightly. The guinea-pig receiving the usual dose had but slight lesions after fifty-eight days. The one receiving twice the usual dose died in eighteen days.

Human Culture XV.

The material from which this culture was isolated was sent to me by Dr. Warfield T. Longcope, of Philadelphia, at the suggestion of Dr. Simon Flexner. The case was that of a negro cook, aged thirty-nine, admitted to the Pennsylvania Hospital April 26, 1903. He had been taken ill with cough about two weeks before admission. Of the results of the clinical examination only the following points need be mentioned: Fine crepitations and rhonchi over the lungs; heavy precipitate of albumin in the urine; sputum free from tubercle bacilli. Death ensued on the eighth day. During the disease the temperature was elevated and irregular, ranging from 101° to 104° F.

The following abstract of the autopsy protocol was kindly forwarded to me by Dr. Longcope:

Anatomical Diagnosis. Acute disseminated miliary tuberculosis, caseation of mesenteric lymph glands, tuberculosis of lateral ventricles of brain, tuberculosis of thoracic duct, acute splenic tumor, cloudy swelling of liver and kidneys, acute aortic endocarditis.

Peritoneal cavity normal. Pleural surface covered with miliary tubercles. Pericardium normal.

Heart. On two of the cusps of aortic valves there are several delicate gray and yellow granular vegetations which are distributed along the point of closure of the valves beneath the vela. The aortic as well as the other valves are thin and delicate. No other marked changes in heart.

Lungs. Slight chronic fibrous pleurisy; pleura everywhere sanded with minute miliary tubercles. On section the cut surface of both lungs is seeded with small gray and yellow tubercles. Very few exceed pin-head in size, but some in upper lobe of left lung are caseous, and are 2 to 4 mm. in diameter. There are no cavities, old scarred areas, or evidence of chronic tuberculosis.

Spleen. Weight, 170 grams. It is filled with miliary tubercles.

Liver. Cut section seeded with fine pin-point gray tubercles.

Kidneys. Many tubercles scattered over capsule and cut sections. They are gray and yellow, and measure from 2 to 3 mm. in diameter.

Pelvis and ureters normal. No lesions found in stomach, *intestines*, urinary bladder, prostate, seminal vesicles, or testes.

Mesenteric glands average 2 to 3 cm. in diameter. Most of them are either entirely caseous or contain large areas of caseation. Retroperitoneal glands are enlarged, but show no caseation. Thoracic duct thickened throughout. Near the receptaculum chyli the lumen is partly filled with soft caseous material. The walls of the duct are everywhere studded with gray or yellow tubercles.

In this case, as in the preceding one, the evidence that the tubercle bacilli entered by way of the intestines was pretty definite, and hence an effort was made to isolate the bacillus. The material sent to me was a piece of lung tissue. It contained, besides many tubercle bacilli, a variety of other bacteria. Three guinea-pigs receiving intraperitoneal injections of salt solution in which the lung tissue had been torn up died within twelve hours. An effort was next made to remove the miscellaneous bacteria by washing the remaining tissue repeatedly in sterile salt solution. After this treatment stained preparations of the tissue showed only a very large number of tubercle bacilli. These were either straight or slightly bent rods fully 4μ long. A few were fragmented.

A second lot of guinea-pigs were inoculated with the washed tissue, two into subcutaneous pockets with bits of tissue, a third with a suspension into the peritoneal cavity. All remained alive until chloroformed after twenty-five or thirty-five days. The disease ran a mild course, and when chloroformed all the guinea-pigs had gained considerably in weight. Successful cultures were obtained from each guinea-pig. The bacilli grew in the form of large isolated or confluent colonies of a smooth, glistening appearance on dog's serum. Subcultures on glycerin agar and in glycerin bouillon were readily obtained, and after several generations the appearance of the cultures differed nowise from the human type of bacilli.

In form they varied in length from 1 to 3μ, the greater number being 1.5 to 2μ long, slightly curved.

TABLE I.—RABBITS. (All inoculations are into an ear vein.)

Designation of culture.	Total age of culture.	No. of transfer.	Age of culture used.	Dose in c.c.[1]	No. of rabbit.	Date of inoculation.	Initial weight (grams)	Final weight (grams)	Result.	Remarks.
Human XIII.	28 days.	Second	10 days	1.00	104	Apr. 25, 1903	2970	2992	Chloroformed after 2 months.	Very fat; foci in kidneys; barely visible tubercles in liver; lungs free.
" XIII.	28 "	Second	10 "	0.5	171	Apr. 25, 1903	1648	1870	Chloroformed after 2 months.	A few foci in kidneys; some minute tubercles in lungs.
" XIV.	35 "	Second	9 "	1.00	138	May 2, 1903	2548	1995	Chloroformed after 1 month.	Because of discharge from nostrils ("snuffles"); considerable number of small tubercles in kidneys; a few minute tubercles in lungs.
" XIV.	35 "	Second	9 "	0.5	172	May 2, 1903	1625	1540	Chloroformed after 54 days.	Many foci in kidneys; none in lungs; tubercles in iris of both eyes.
" XVa.	3 months 18 days.	Fourth	10 "	0.75	132	Oct. 3, 1903	1990	2455	Chloroformed after 3 mos. 12 days.	Moderate number of foci in kidneys; none in lungs.
" XVc.	3 months 8 days,	Third	10 "	0.4	180	Oct. 3, 1903	1975	2245	Chloroformed after 2 mos. 4 days.	A very few gray tubercles in kidneys and lungs.

[1] The suspension in normal salt solution is, as heretofore, equivalent in density to a twenty-four-hour bouillon culture of typhoid bacilli after removal of clumps by sedimentation. Dog serum was the culture medium.

TABLE II.—GUINEA-PIGS. (All inoculations are intra-abdominal.)

Designation of culture.	Total age of culture.	No. of transfer.	Age of culture used.	Date of inoculation.	Dose in c.c.	Initial weight (grams)	Final weight (grams)	Result.	Remarks.
Human XIII.	28 days	Second	10 days	Apr. 25, 1903	1.00	319	234	Died in 52 dys.	Lymph nodes not affected; spleen large; no visible tubercles in lungs, liver, and spleen.
" XIII.	28 "	Second	10 "	Apr. 25, 1903	0.5	301	260	Died in 48 dys.	Like preceding.
" XIV.	35 "	Second	9 "	May 2, 1903	1.00	375	300	Died in 18 dys.	Multiple necrotic foci in liver; spleen large; lungs not affected; lymph nodes barely so.
" XIV.	35 "	Second	9 "	May 2, 1903	0.5	379	325	Chloroformed in 58 days.	Spleen large; no visible tubercles in any organ, except on testicles.
" XVa.	3 mos. 18 dys.	Fourth	10 "	Oct. 3, 1903	0.5	397	....	Died in 50 dys.	Lungs filled with tubercles; liver and large spleen free.
" XVc.	3 mos. 8 dys.	Third	10 "	Oct 3, 1903	0.5	410	270	Died in 18 dys.	Hyperplasia of omentum; multiple necrosis in liver; lungs compressed by effusion; no visible tubercles; pregnancy discovered after inoculation.

TABLE III.

Composition of bouillon.	Designation of culture.	Date of inoculation.	Reaction of bouillon in per cent. of a normal solution after (— = acid, + = alkaline).
No. 1111.[1] One per cent. Witte peptone; three per cent. glycerin. Reaction — 2.05. Moderate amount of muscle sugar.	Bovine VIII.	May 8, 1903	35 days = — 1.05; 48 days = — 0.75; 81 days = — 0,6.
	Human XII.	" 8, "	35 " = — 1.65; 48 " = — 1.6; 81 days = — 2.1.
	" XIII.	" 8, "	35 " = — 1.65; 81 " = — 1.45.
	" XIV.	" 8, "	35 " = — 1.6; 81 " = — 1.65.
	" XVa.	Sept. 29, " [2]	49 " = — 1.3; 85 " = — 1.6.
No. 1132. Same composition as above. Reaction = — 1.8. Trace of muscle sugar only.	Bovine VIII.	June 22, 1903	71 days = — 0.3; 94 days = — 0.15.
	Human XII.	" 22, "	71 " = — 1.7; 94 " = — 2.25.
	" XIII.	" 22, "	71 " = — 1.15; 94 " = — 1.00.
	" XIV.	" 22, "	71 " = — 1.8; 94 " = — 2.1.
	" XVa.	Sept. 29, " [2]	63 " = — 1.2; 89 " = — 1.6.
No. 1153. As above. Reaction = — 1.8. Slight amount of muscle sugar.	Bovine VIII.	Sept. 18, 1903	31 days = — 0.25; 60 days = — 0.0; 96 days = — 0.0.
	Human XIII.	" 29, "	30 " = — 0.8; 62 " = — 6.5; 86 " = — 0.75.
	" XIV.	" 18, "	60 " = — 0.85; 99 " = — 1.65.
	" XVB.	" 18, "	53 " = — 1.00; 85 " = — 2.35; 99 " = — 2.45.
	" XVc.	" 29, "	31 " = — 1.00; 63 " = — 2.5; 89 " = — 2.85.

[1] This lot of bouillon was unfavorable for some unknown reason, for the membrane of the various cultures remained comparatively feeble. This probably accounts for the cessation of growth of Bovine VIII. before approaching the zero point

[2] These flasks were more or less concentrated by evaporation at the date of inoculation.

For the virulence and culture tests two strains from two different guinea-pigs, denominated respectively XVa. and XVc., were saved. The effect of this tubercle bacillus in pure culture, even in twice the doses usually given, was that of a highly attenuated type, as shown in Tables I. and II. It will be noticed that one guinea-pig was pregnant at the time of inoculation. This condition, unknown at the time, was probably the cause of the early death as compared with the mate inoculated with the other strain of bacilli. The second animal lived a long time in spite of the fact that the inoculation was intra-abdominal.

In the rabbits the disease was very mild and the lesions limited to a few foci in the kidneys of both and a few translucent tubercles in the lungs of one. The one receiving 1½ times the standard dose gained nearly 500 grams in three months.

The Reaction Test in Glycerin Bouillon.

In a preceding paper[1] the writer called attention to the difference in the movement of the reaction of the glycerin bouillon in which bovine and human bacilli are multiplying. In the case of the bovine cultures this movement leads to a final reaction, either neutral, feebly alkaline, or feebly acid, toward phenolphthalein; in case of the human cultures to a pronounced acidity to phenolphthalein. In the latter the reaction at first becomes less acid, then either much more acid, or else it remains at a medium level. Concerning various precautionary details in applying this test to cultures, the reader is referred to the earlier paper.

In Table III. the tests made with the three new cultures are given in detail. Three different lots of glycerin bouillon were tried, and for controls two older cultures, Bovine VIII. and Human XII., were studied side by side with the new ones.

The first lot of glycerin bouillon, No. 1111, was, for some unknown reason, opposed to a very active growth of the bacilli. The membranes remained thin and smooth, and as a result the alkali production in Bovine VIII. was feeble and inhibited after a time. This case, the first I have encountered, suggests caution in interpreting results until several lots of bouillon have been tried.

The titrations yielded results which agree essentially with those tabulated in the preceding paper. The reaction of the bovine culture in the three lots of bouillon moves gradually to the phenolphthalein neutral point. The human cultures pursue one of two courses. They either attain a greater than the initial acidity after two or three months (Human XII., XIV., XVa. and XVc) after having become less acid, or else, as in Culture XIII., the reaction remains after some preliminary fluctuation at a medium level of acidity.

[1] Transactions of Association of American Physicians, 1903, vol. xviii. pp. 109–151.

These changes in reaction have already been discussed and referred to glycerin as the cause. Further investigations on this subject are now in progress.

Summary.

The bacilli isolated from these three cases of presumable food infection do not correspond to the bovine type of bacilli in any one particular.

1. They were readily cultivated from nearly all the guinea-pigs inoculated, and they grew luxuriantly from the start on dog's serum. Subcultures on glycerin agar and glycerin bouillon grew vigorously after the first transfer from dog's serum.

2. Morphologically the bacilli were either fairly long—*i. e.*, they averaged about 2μ in length, or else they were very variable, polymorphic. The uniformly short, straight forms of the bovine type were absent.

3. In all cases the bacilli were of a very low order of virulence, lower even than that of many of the cultures of human origin studied heretofore.

4. None presented the reaction curve of true bovine bacilli.

We have, as yet, no satisfactory evidence concerning the degree of change, if any, which tubercle bacilli of bovine type may undergo in the human body. That changes could be as thoroughgoing as would be the case if we were inclined to attribute these cases of infection by way of the digestive tract to milk is at present quite inconceivable, and we must content ourselves by referring them to infection with bacilli of strictly human origin.

A STUDY OF CIRCUMSCRIBED AND DIFFUSE PULSATION OF THE WALL OF THE THORAX.

WITH THE REPORT OF A CASE OF PULSATING HÆMOTHORAX.

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Pulsation of the wall of the thorax is a physical sign varying so much in extent and degree that it is impossible to ascribe to it any general significance. Premising that it is invariably due to pulsation transmitted from the heart or large bloodvessels, with the exception of an apparent, not a real, pulsation due to rhythmical muscular contractions, the only classification that is possible is (1) pulsation without structural alteration in the walls of the thorax or in the tissues lying between the walls and the heart and bloodvessels, and (2) pulsations in which these structural changes exist and may be

supposed to be the transmitting agents. In the former group are included all those forms of pulsation due to increase in the activity of the heart, where this increase is due to structural alteration or functional conditions, such as increased muscular activity or irritability of the nerve supply. It is hardly necessary to speak of the former group; pulsation of the wall of the chest is common in cases of marked hypertrophy of the heart. It may be limited to the precordial region, or cause a general systolic shock in a large area of the wall of the chest, perhaps extending along the upper part of the abdomen. The systolic movement is often wave-like in character, appearing to follow the heart's contraction from the base toward the apex, and this wave often appears to continue beyond the apex, moving toward the abdominal wall. Sometimes the impulse is more distinct to the eye than the hand. It may reach its maximum intensity in the region of the apex of the heart, and not infrequently is associated with slight bulging of the precordium. The impulse that occurs after violent exertion or excitement is usually characterized by a general systolic shock involving the whole of the thorax, and sometimes causing a movement of the trunk and head. Pulsation, either localized or diffuse, may occur in thoracic aneurysms. These varieties are sufficiently familiar to be passed without further comment.

Another form of pulsation occurs the nature of which is not quite so clear. The following case was observed at my clinic at the Polyclinic Hospital:

L. J., a Russian Jew, aged twenty-six years. The heart was normal and not beating vigorously. There was distinct suprasternal pulsation; the abdominal aorta pulsated palpably and visibly; there was distinct negative pulsation in the veins of the shoulder, which were distended, but no diastolic pulse was present in the veins at the base of the neck. Pulsation of the liver could not be determined, and the organ was not enlarged below the border of the ribs. There were no signs of arteriosclerosis. *There was a distinct, though slight, systolic pulsation of the whole right side of the thorax.* This was not perceptible upon palpation, probably because it was too diffuse. The left side did not pulsate. There were no signs of pleural effusion on the right side. The pulmonary sounds were normal, and the percussion note was not impaired. The patient had a slight degree of gastroptosis.

In a somewhat similar case recently reported by Edwards, there was vigorous expansile pulsation on the left side near the base, which led to the suspicion of aneurysm of the aorta. At the autopsy the thoracic organs were found to be entirely normal, but the blood-vessels were atheromatous. A case has also been observed by La Fleur.

In the case I report I am led, for lack of any more satisfactory explanation, to suppose that the pulsation of the thorax was similar

to that observed in the abdomen, and was possibly due to the rather voluminous pulse not infrequently present in persons with long, narrow thoraces and ptoses of the organs.

Of the abnormal pulsations in the wall of the thorax, due to organic changes, perhaps the most common and important is the systolic retraction that may be associated with pericardial adhesions. The most pronounced form is that in which, in addition to the retraction of the apex, there is also retraction in the epigastrium and in the lower interspaces in the left posterior axillary line, known as Broadbent's sign. This sign is not uncommon. I have observed it in several cases, but upon only one of these could an autopsy be obtained. This case was as follows:

W. L., aged forty-two years, had had syphilis and rheumatism. He had known that he had heart trouble for five or six years. The area of cardiac dulness extended from the right parasternal line to the left anterior axillary line. There was a loud, harsh murmur at the apex, systolic in time, not heard at the base. There was pulsation in the veins of the neck, and a pulsating liver throughout the entire time of observation, which was three years. There was systolic retraction at the apex and epigastrium, and also in the eighth, ninth, tenth, and eleventh interspaces posteriorly. The latter was very distinct, and served on numerous occasions for the demonstration of Broadbent's sign.[1] A diagnosis was made of mitral and tricuspid regurgitation and obliterative pericarditis. At the autopsy the heart was found lying horizontally in the thorax, and extending from the right anterior axillary line to the left posterior axillary line. The left auricle was enormously dilated, being about as large as the rest of the heart. There was a buttonhole mitral valve, a greatly dilated tricuspid orifice, and obliterative pericarditis and pleuritis.

Next in importance are the cases in which effusion of air or liquid or both has taken place into the pleural cavity. This forms by far the most interesting group, and will, therefore, require more extended consideration. The condition has been known since the oft-quoted case of De Baillou, which was reported in 1640. It was evidently seen by others, and was fairly well known in the eighteenth century, if we may judge from the remarks in Le Roy's *Aphorisms*. The first case, however, that was ever reported with any degree of accuracy, according to Comby, is that of Bérard, which was published in 1810. Later, MacDonnell, independently

[1] Broadbent's patient was a girl of nineteen who had been sick for two months. She was brought to the hospital two days before her death, with signs of pleural effusion on the left side. The heart was displaced to the right, but there was visible and palpable pulsation from the fifth interspace in the left nipple line to the xiphoid cartilage, and also in the tenth interspace from the spine to beyond the angle of the scapula. An aneurysm or malignant tumor was suspected, but at the autopsy obliterative pericarditis with adhesions of the pericardium to the central tendon of the diaphragm and the chest wall was found. Broadbent suggested that the pulsation posteriorly was due to the tugging of the heart on the diaphragm.

and in ignorance of Bérard's work, published three interesting observations, and Stokes published one, reported most unsatisfactorily, and yet, on account of the extraordinary character of some of the symptoms, particularly noteworthy. A number of other cases were subsequently published, some complete, some merely mentioned incidentally in the course of the discussion of other conditions. Finally, in 1883, Comby, in addition to reporting three cases of his own, made a careful study of the literature and was able to collect twenty-seven cases all told. Four years later Keppler also reviewed the literature, reporting one case of his own, and collecting 38 cases. In 1888 Rummo reported 2 cases and reviewed the literature. In 1895 Comby published a small monograph in which he described 47 cases. In 1897 Fuchs reported an additional case, and was able to find 13 other cases not in Keppler's collection, bringing the number up to 52 cases. In the mean time, however, Wilson, of Philadelphia, in 1893, had reported 3 cases that had come under his observation, and had collected 65 cases from the literature, including those reported by Comby and Keppler. In 1900 Innocenti and Marsili reported 2 cases, and gave a careful review of the literature. Then, in 1903, Henry made a final report of his case, and added 15 cases not in Wilson's collection, making the total 80 cases. As far as I can discover, the total number of cases on record is 97, of which several are so incompletely reported that they are worthless for statistical purposes.

From a study of these cases we can recognize the following groups: (1) pulsating empyema and pulsating pyopneumothorax of necessity; (2) pulsating empyema and pulsating pyopneumothorax; (3) pulsating encapsulated empyema; (4) pulsating serous or hemorrhagic effusion; (5) pulsating extrapleural abscess.

The frequency of pulsations associated with various forms of pleural exudate is probably not great. Comby suspected that it was often overlooked, but after his excellent paper had called general attention to the subject the number of such cases reported was not very materially increased. Thus in Paris only four additional cases were observed in the period from 1882 to 1895. The condition may now be regarded as fairly well known. Several critical papers have been published in France by Comby; in Germany by Keppler and Fuchs; in America by Wilson and Henry; in Italy by Rummo and Innocenti and Marsili, and in England by West. Toft observed it in about 3 per cent. of his cases of empyema. Innocenti and Marsili estimate its frequency at 1 per cent. Many clinicians of large experience, as Millard, who have seen one case, and whose attention has been aroused, have not seen others, and other clinicians who have written about the subject, such as Rosenbach,[1]

[1] Diseases of the Bronchi, Lungs, and Pleura, edited by J. H. Musser, Philadelphia, 1902, p. 896.

von Leube[1] and West have never observed any cases. It may be assumed, therefore, that such pulsations are uncommon, and must be produced by some unusual condition or group of conditions. Although these conditions must occur more or less independently of the nature of the pleural exudate, nevertheless the phenomena produced vary considerably in the different forms, and I believe it will be advisable to consider them separately. Before doing this it is well to discuss the different varieties of pulsation that may occur.

It has been customary to divide the visible and palpable pulsations into those more or less diffuse in character and without tumor formation, and those in which a definite pulsating tumor occurs. Both may be present simultaneously in the same case. As the term "empyema of necessity" (pointing empyema) implies, tumors may appear in the wall of the thorax, and the pulsation may be limited strictly to them. It is, in fact, such tumors, often mistaken for aneurysm, that constituted the majority of the early reports of this condition, and gave rise to the belief, first expressed by Comby, that pulsation only occurs when the exudate is purulent. The pulsation in these tumors is systolic in time, that is to say, all observers, with the exception of MacDonnell and Stokes, state that it is synchronous with the contraction of the heart or with the pulse in the great vessels. MacDonnell states that in all his cases the pulsation was diastolic, but he does not say whether he compared it with the contraction of the heart or the pulsation of the radial artery, and it is improbable that in his cases it differed in character from that observed in the others. There is some question as to whether or not the pulsation is expansile. Ordinarily it is so described; but Duplay, who saw a case of Comby's in consultation, was able to demonstrate that it was not of the true expansile type observed in aneurysmal pulsation. Ordinarily the maximum pulsation is observed at the apex of the tumor, and not infrequently, when more than one tumor is present, one will pulsate and the other or others remain motionless. In some cases the pulsation does not develop *pari passu* with the tumor, but appears more or less suddenly sometime in its course, as in the case reported by Heyfelder. In other cases the pulsation is variously affected by different therapeutic measures that may be employed.

Rummo lays particular emphasis upon the difference between endopleural and exopleural pulsation. By the latter he means a pulsation that is visible and palpable externally, and by the former pulsation in a pleural exudate that can be detected only by instruments. For this purpose he used a hollow needle, a rubber tube, and a mercurial manometer, or, when the graphic method was employed, the tambour of a Marey sphygmograph. Then thrusting

[1] Diagnose der inneren Krankheiten, Leipzig, 1902, Bd. 1. p. 175.

the needle into the pleural cavity he was able to get a tracing of the pulsation occurring in it. I have tried this three times, once in right-sided pleural effusion, and twice in left-sided pleural effusion, but have been unable to observe pulsation synchronous with the heart. I think it must be obvious that the distinction between the endopleural and exopleural pulsations is one rather of degree than of kind. If the endopleural pulsation becomes slightly stronger it will become exopleural without any change in the causative conditions. The classification of West, therefore, appears to be more satisfactory. He recognizes three forms: first, a general systolic shock over the thoracic wall, occurring in large effusions with much pressure; very much the same, he says, as the pulsation which may be transmitted through an intrathoracic tumor or the solid lung in pneumonia; second, a pulsation felt usually in front, which is due to the propagation through the fluid of a wave, and to relaxation of the walls of the thorax; third, an expansile type of pulsation which resembles the fluctuation observed in abscesses, and to produce which the surrounding portions must be rigid. The objection to West's classification is, I think, that it depends upon a hypothetical etiology. Clinically, I believe that a more satisfactory classification is as follows:

First. The diffuse pulsations of the thoracic walls. Of these there are two forms: first, a perceptible and palpable or merely palpable pulsation felt in one part of the thoracic wall. This gives a sensation not unlike that communicated by the wave that travels through an ascitic accumulation of fluid, but ordinarily not quite as distinct. In a case of chronic tuberculous empyema that I had an opportunity of observing in Dr. Allyn's wards at the Philadelphia Hospital I was able to demonstrate this form of pulsation to my class. It was felt from the eighth to the eleventh interspaces in the neighborhood of the posterior axillary line on the left side. It was not a pronounced pulsation and was not visible. The second form is a more powerful pulsation affecting the whole wall of the chest, visible and palpable, and even perceptible subjectively to the patient. The most remarkable case of this kind is that reported by Stokes, one of the earliest cases of pulsating pleurisy to become generally known. In this case the pulsation was so violent that it not only kept the patient awake at night, but even perceptibly shook the bed, and this in spite of the fact that the cardiac action was not greatly exaggerated. One of Béclère's cases exhibited the same form of pulsation.

Second. The circumscribed pulsations with tumor formation. These may be subdivided into four classes: first, cases of empyema or pyopneumothorax, in which, as a result of a local area of weakness, there is a bulging of the wall of the thorax where the pulsation occurs; second, the cases in which there has been perforation of the pleura, the pus from the empyema passing through the intercostal

muscles, and giving rise to a subcutaneous abscess communicating with the empyema by a fistula. In both these classes there may also be diffuse pulsation; third, localized bulging and pulsation as a result of encapsulation of fluid in the pleural space, whether the fluid is purulent or serous in character; fourth, the formation of an abscess entirely outside of the thoracic cavity, usually arising from the periosteum of the ribs or sternum, and ordinarily tubercular in nature. Such tumors are comparatively rare. I have already discussed and illustrated the non-pulsating form in a previous paper.[1] Unless perforation from without inward has occurred it is difficult to understand how the pulsation is produced.

Third. A true expansile pulsation of the whole thorax, of which the only certain case apparently is the one I record, that is probably due in part to factors other than the mere accumulation of fluid in the pleural cavity, the displacement of the viscera, and the altered tension of the walls.

Rather than give brief abstracts of all the reported cases—which has already been done satisfactorily in this country by Wilson and continued almost to date by Henry—it has seemed to me more useful to summarize the results in the form of statistics. In order, however, to avoid the imputation of including imaginary cases, most unjustly made of Wilson by Fuchs and Innocenti and Marsili, I shall give a list of the references of all the cases I have been able to collect, arranged chronologically. These are altogether ninety-seven. Two of these cases (Potain and West) are mentioned incidentally in the discussion, in one instance of pulsating empyema, in the other of thoracic aneurysm. No details whatever are given, and they are, therefore, not considered. It has been customary since Keppler's paper appeared to include the case of Geigel[2] in the group of pulsating empyemas. In his report, however, Geigel states that the tumor below the ribs on the right side gave a distinct sense of fluctuation, but says nothing of pulsation. The case, therefore, has been omitted.

Woillez[3] mentions cases observed by Koelpin and Govelle, but Comby has been unable to find the original records:

Baillou. Empyema of Necessity. Paris, 1640. Quoted by Comby.

Pelletan. Extrapleural Abscess. Clinique chirurgicale ou mémoires et observations de chirurgie clinique, Paris, 1810, tome iii. p. 254.

Bérard. Empyema of Necessity. Du diagnostic dans les maladies chirurgicales de ses sources et de ses incertitudes et de ses erreures, Paris, 1836.

MacDonnell 1. Pyopneumothorax with Tumor. 2. Empyema of Necessity. 3. Empyema of Necessity. Dublin Journal of Medical Sciences, 1844, p. 1.

Wintrich. 1. Empyema of Necessity. 2. Empyema of Necessity. Virchow's Handbuch der speciellen Pathologie u. Therapie, 1854, Bd. v. pp. 259–301.

Stokes. Empyema. Diseases of the Heart and Aorta, Dublin, 1854, p. 607; Philadelphia, p. 623.

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[1] Philadelphia Medical Journal, April 5, 1902.

[2] Wurzburger med. Zeitschr., 1859, Bd. i.

[3] Traité clinique des maladies aiguës des organes respiratoires, Paris, 1872, p. 403.

Vidal. Mediastinal Abscess. Bull. de la Société anatomique, 1854, 29th year, p. 243.
Cruveilhier. Serous Effusion. Bull. de la Société anatomique, 1854, p. 244.
Asson. Empyema of Necessity. Giornale veneti di Scienze med., September, 1855.
Flint. Serous Effusion. Physical Exploration and Diagnosis of Diseases Affecting the Respiratory Organs, Philadelphia, 1856, p. 581.
Heyfelder. 1. Empyema of Necessity. 2. Circumscribed Pleural Abscess. Zeit. f. praktische Heilkunde, November, 1858, p. 860.
Aran. Empyema of Necessity. Gazette des hôpitaux, November, 1858, No. 108, p. 91.
Rees. Empyema of Necessity. British Medical Journal, August 21, 1858.
Wilks. Empyema of Necessity. Lancet, November 12, 1859, p. 481.
Baly. Serous Effusion. Lancet, November 12, 1859, p. 482.
Wiltshire (Chandler). Empyema of Necessity. Lancet, May 31, 1862, p. 573.
Chambers (Ash). Empyema of Necessity. Lancet, May 31, 1862, p. 573.
Lesage. Circumscribed Empyèma (Empyème pulsatil à répétition). Gazette des hôpitaux, October 31, 1865, p. 511.
Chvostek. 1. Empyema of Necessity. 2. Empyema of Necessity. 3. Empyema of Necessity. Wiener med. Blätte, 1865, p. 115.
Reyher. Periosteal Abscess. Berl. klin. Woch., 1868, p. 426.
Courbon (Le Double). Empyema of Necessity. Gazette des hôpitaux, May 24, 1870, p. 237.
Toft. 1. Empyema of Necessity. 2. Empyema of Necessity. 3. Empyema. Nord. med. Arkiv, 1871, Bd. iii., No. 7.
Walshe.[1] 1. Empyema. 2. Empyema. Practical Treatise of Diseases of the Lungs and Heart, 4th edition, 1871, p. 296.
Kemp. Empyema. Quoted by Walshe.
Traube. 1. Doubtful. 2. Empyema. Berl. klin. Woch., 1872, No. 7.
Shattuck. Empyema. International Clinics, January, 1872, p. 87.
Plagge. Empyema of Necessity. Beiträge z. Kenntniss d. pulsirenden Thoraxgeswulste. Memorabilien, 1872, No. 11, p. 481.
Müller. Empyema of Necessity. Berl. klin. Woch., January 22, 1872, p. 37.
Fraentzel. Empyema. Ziemssen's Handbuch, 1874-75, Bd. iv. 2d half, p. 301.
Lorenzutti. Empyema of Necessity. Annali universali di medicina e di chirurgia. Milano, 1875, vol. ccxxxii. p. 385.
Topham. Intrathoracic Abscess. Lancet, 1878, p. 756.
Dunin. Doubtful. Gazetta Lekarska. Quoted by Comby.
Brünniche. Extrapleural Abscess Communicating with Empyema. Hospitalstidende, 2 R., Bd. ix. p. 65; Virchow-Hirsch Jahresberichte, II., 1882, Bd. x. p. 146.
Comby. 1. Empyema. 2. Empyema. 3. Empyema. 4. Empyème (case of Duguet). Arch. générale de médecine, 1882, p. 549; l'empyème pulsatile, Paris, 1895.
Yeo. Empyema of Necessity. Lancet, February 23, 1884, p. 331.
Dillingham. Empyema. New York Medical Record, March 8, 1884.
Féréol. Pyopneumothorax. Proc. de l'acad. de médecine, 1884, No. 7, p. 155.
Broadbent. Serous effusion. Lancet, May 31, 1884, p. 971.
Pel. Circumscribed Empyema. Berl. klin. Woch., February 25, 1884, p. 113.
Ross. Circumscribed Empyema. Canadian Medical and Surgical Journal, May, 1885, p. 606.
Henry. Pyopneumothorax with Tumor. Proceedings of the Philadelphia County Medical Society, 1885, vol. iii.; New York Medical Journal, May, 1903.
Florand. Empyema. La France médicale, 1886, p. 158.
Codivilli. Empyema of Necessity. Thesis, Bologna, 1886, No. 97. Quoted by Rummo.
Cammareri. Empyema of Necessity. Gazetta degli Ospedali, 1886, No. 97, p. 772.
McCosh. Empyema of Necessity. Medical Record, January 30, 1887, p. 156.
Keppler. Circumscribed Pleural Effusion. Deutsche Archiv f. klinische Medicin, 1887, p. 220.
Borgiotti. Pyopneumothorax. Clin. med. in Bollet. de Soc. Cult. d. Scienzi Siena, 1886-87, p. 91.
Rummo. 1. Empyema. 2. Empyema. Riforma Medica, 1888, p. 1304.
Martinez. Seropneumothorax. Quoted by Rummo.
Millard. Empyema of Necessity. Gazette hebdom. d. méd. et de chirur., 7-12, 1899, p. 447.
Osler. Serous Effusion. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, January 1889, p. 43.
Martin. Pyopneumothorax with Tumor. Revue méd. de la Suisse Romande, 1889, No. 2.
Bimmerman. Empyema. Geneeskundig Tydschrift voor Nederlandsch Indië, 1889, Bd. xviii. Quoted by Henry.

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[1] Walshe states that he has seen six cases altogether.

Monari. Empyema of Necessity. Gaz. degli Ospedali, August 6, 1890, No. 63, p. 498

Light. 1. Empyema of Necessity. 2. Empyema of Necessity. 3. Empyema of Necessity. Lancet, September 26, 1891, vol. ii. p. 704.

Wilson. 1. Pyopneumothorax with Tumor. 2. Empyema. 3. Pyopneumothorax. Transactions of the Association of American Physicians, Philadelphia, 1893, vol. viii. ; Medical News, July 15, 1893.

Pittorelli. Empyema. Gaz. degli Ospedali, 1893, vol. xiv. p. 1260.

Watkins. Pyopneumothorax. Lancet. Jannary 21, 1893, p. 133.

Osler. Pyopneumothorax. Transactions of the Association of American Physicians, 1893, p. 210. Discussion of Wilson's paper.

Potain. Extrapleural Abscess. Médecine moderne, November 29, 1893.

Béclère. 1. (Marieux) Empyema. 2. (Béclère's) Empyema. Bull. et mém. de la Société. médicale des hôpitaux de Paris, 1894, tome xi. p. 339 ; tome xii. p. 42.

Proust. Empyema. Ibid., 1894, p. 339.

James. Empyema of Necessity. International Clinics, 1895, vol. ii. p. 5.

Toulmin. Empyema of Necessity. University Medical Magazine, 1895, vol. vii. p. 853.

Roux. Empyema. La Province médicale, Lyon, 1896, tome x. p. 100.

Lepine. Serous Effusion. Lyon médicale, 1896, No. 8, tome lxxxi. ; Centralbl. f. innere Med., 1897, p. 765.

Fuchs. Pyopneumothorax. Zeitschr. f. klinische Medicin, 1897, 32 Suppl. Hft., p. 255.

Sallés. 1. Pyopneumothorax. 2. Pyopneumothorax. La Province médicale, 1897, tome xi. p. 337. Quoted by Henry.

Cavazzani. Extrapleural Abscess. Gaz. degli Ospedali, 1897, vol. xii. p. 781.

West. Extrapleural Abscess. Medical Chirurgical Transactions, 1897, vol. lxxx. p. 239.

Innocenti and Marsili. 1. Empyema. 2. Hæmopyothorax. Riforma Medica, 1900, No. 261, p. 423.

Auerbach. Serous Effusion. Münchener med. Wochs., 1901, p. 1228.

McPhedran. Serohemorrhagic Effusion. Transactions of the Association of American Physicians, 1903, p. 334.

Kullman. Serous Effusion. Deut. med. Woch., 1904, p. 339.

Stanton. Empyema of Necessity. Unpublished. Read before the Medical Section of the College of Physicians of Philadelphia, 1904.

Sailer. Hæmothorax.

The attempt to classify the cases is only partially successful, but the following list appears to be approximately correct:

Cases of	empyema of necessity, that is, with tumor formation	34
"	pyopneumothorax with tumor formation	4
"	empyema without tumor formation	25
"	pyopneumothorax without tumor formation	8
"	serous or hemorrhagic effusion	12
"	circumscribed empyema	5
"	extrapleural abscess	5
"	uncertain nature	2

Properly speaking, then, we have of the cases with pus in the pleural cavity, 38 with tumor and 33 without tumor. There were 13 cases of intrapleural or extrapleural abscess, and the remaining cases were either non-purulent or their nature not definitely known. It is not at all impossible that some of the cases of supposed serous pleurisy may have been purulent. This is particularly true of the case reported by Flint, and it is certain that in one case (Keppler's) the fluid, which was clear at the time of the first puncture, subsequently became purulent.

Of the 95 cases, 63 were males 19 females, and in 13 the sex is not given. There are, therefore, nearly three and one-half times as many males as females. Twelve patients were under twelve years of age; 10 between the ages of ten and twenty; 32 between twenty

and thirty; 14 between thirty and forty; 6 between forty and fifty; and 3 between fifty and sixty. In 18 the age is not given. Practically 90 per cent. of the cases occurred before the age of forty, and nearly 70 per cent. before the age of thirty. Pulsation of the wall of the thorax may therefore be regarded as distinctly a condition of early life. The youngest case (Light) was three years, the oldest (Cavazzani) was fifty-six years.

The only interest in the result of these cases is in determining whether pulsation increases the gravity of the prognosis or not. Of the 95 cases, 37 recovered, 27 died, 16 were improved (probably in many cases only temporarily), and in 20 the result is not stated, either because the report was made while the patient was still under observation, because the patient withdrew from observation, or because the case was mentioned incidentally with reference only to the pulsation. Therefore, the mortality of the cases whose termination is definitely known is 46.7 per cent. The following table shows the results for the different forms:

	Recovered.	Died.	Improved.	Not stated.
Empyema with tumor	11	10	6	7
Empyema without tumor	6	8	4	7
Pyopneumothorax with tumor	1	3	0	0
Pyopneumothorax without tumor	2	1	4	1
Serous effusion	4	3	2	3
Circumscribed empyema	3	1	1	0
Extrapleural abscess	3	2	0	0

It is hardly worth while to note the manner in which the cases were treated. Operations were performed upon 69 cases, and in 6 of these spontaneous rupture also occurred. Spontaneous rupture into the lung occurred three times, into the œsophagus once, and externally six times. No treatment was employed in 6 cases, and in 11 the reports do not furnish any information. The operations included practically all the operations for empyema: aspiration, drainage, or resection of one or more ribs. In the case of Bérard the patient punctured the supposed aneurysm with a needle. Topham's patient was kept in bed for three years before spontaneous rupture occurred. The majority of cases that recovered had persistent deformity, but in a few cases the thorax resumed its normal shape.

The position of the heart is of some interest. It is stated that it was displaced to the right in 53 cases, in all of which the lesion was on the left side. In 31 left-sided cases its position is not mentioned, but often it is obvious that it must have been displaced. In 3 right-sided cases its position was not mentioned. In 1 right-sided case (Borgiotti) it was displaced to the left. The degree of displacement varied considerably. In the case of Wiltshire it was very slightly displaced, but in many of the other cases the apex beat was in the right nipple line, or even beyond that point. It is definitely stated that it was not displaced in 9 cases (Stokes, Vidal, Reyher, Béclère,

Light, Cavazzani, Innocenti and Marsili, Sailer, and McPhedran). Two of these (Vidal and Reyher) were extrapleural abscesses; one (Cavazzani) was apparently a circumscribed empyema. In one (McPhedran) exopericardial adhesions were suspected, but not demonstrated, and in a very remarkable case (Béclère) there was a funnel-shaped thorax extending 3½ cm. inward which prevented the displacement of the heart. For 3 cases (Stokes, Light, and Innocenti and Marsili) no reasons are given, and in the eighth case (Sailer) exopericardial and endopericardial adhesions were found at the autopsy. In the 3 cases reported by Toft, hinderances to the dislocation of the heart, in the form of adhesions or effusion on the right side, existed.

The causes assigned are various, and probably often incorrect. Tuberculosis—in all probability the commonest cause—is mentioned only eleven times, and in only two instances, apparently, confirmed in inoculations (Rummo, Béclère). Acute pleuritis of undetermined nature preceded the condition fifteen times. Chronic pleurisy occurred twice. Pneumonia of some form, with pleurisy or abscess, occurred in 13 cases. There were 4 cases in which an acute illness preceded the empyema. There was 1 case of pertussis. Pleural effusion is said to have been present once. Pneumothorax had apparently been present in one case before the empyema, but had disappeared before the pulsation was observed. Severe injury to the side occurred in 5 cases, exposure twice. In one remarkable instance (Fuchs) there was an attempt at abortion, followed by salpingitis, subdiaphragmatic abscess rupturing through the diaphragm and empyema. A few special cases cannot be grouped. In the case of Courbon there had been dyspnœa and palpitation for four years, with boring pain in the lumbar region. In a case of Innocenti and Marsili, which developed in a man aged forty-three years, there had been pleurisy, with a large effusion at the age of twenty-five. In the case of Martinez carcinoma was present. For some other cases there are merely indefinite statements, such as "pain in the side," "cough," which may indicate an undiscovered pleurisy or pleural effusion, or perhaps pulmonary tuberculosis, and for the rest no etiological factor is mentioned.

The most important part of our knowledge of these conditions is obtained from the records of the autopsies. I will, therefore, give brief abstracts of the post-mortem findings in the 21 cases in which autopsy was performed.

1. MacDonnell: The left lung was collapsed and bound firmly to the chest wall by adhesions; it was tuberculous. The pericardium was adherent to the right lung.

2. MacDonnell: The lungs were tuberculous and contained a large abscess cavity. The fifth and sixth ribs were eroded.

3. Vidal: There was pus in both pleural cavities, and a small pocket back of the sternum, the same size as the tumor and com-

municating with it through a hole. Both these pockets contained thick, creamy pus, and neither communicated with the pleura.

4. Heyfelder: Caries of the second, third, seventh, and eighth ribs; rupture of the pleura, and external empyema. The liver was displaced downward. There was no trace of tuberculosis.

5. Rees: The left side of the chest was retracted; the left lung was compressed and tuberculous; there was also tuberculous meningitis and pneumonia of the right lung.

6. Comby: Tuberculosis of both lungs; fetid gas and pus in the left pleura. The pericardium was adherent to both lungs; the mediastinum was displaced to the left, and the left lung collapsed.

7. Comby: Two litres of pus in the left pleura. The left lung was collapsed and adherent to the pericardium. It contained cheesy nodules. The pleura was not thickened.

8. Comby: The left pleural cavity contained about six litres of pus. The diaphragm was depressed and the mediastinum was displaced to the right. The surface of the pleura was covered with a false membrane. The left lung was solidified and adherent to the pericardium. The membrane covering it was perforated in two places. The right lung was tuberculous. The pericardium was not adherent.

9. Chvostek: The left thoracic cavity was filled with lymph; the left lung was compressed and displaced upward; there were recent pericardial adhesions; the pleura was ruptured in the fifth interspace at the site of the tumor.

10. Chvostek: The left clavicle was dislocated; several ribs were denuded and eroded, and the intercostal muscles were altered. The pleura was thickened and perforated at the site of the tumor; the pericardium was adherent to the tumor, and the lung compressed and solid.

11. Toft: A thick pseudomembrane enclosed the empyema, through which a perforation led to a subcutaneous abscess. The heart was attached to the chest wall. There was obliterative pericarditis and chronic peritonitis.

12. Toft: The left pleural cavity contained pus and air. A fistula communicated with the subcutaneous tumor. The heart was normal. Pus was present in the right pleural cavity.

13. Traube: There was massive purulent pleural and pericardial effusion. At the point of pulsation the pleura was destroyed. The pericardium was thickened; the lung compressed, and the upper lobe was atelectatic. The heart was displaced to the right.

14. Lorenzetti: The lung was adherent to the thoracic wall at several points. There was recent purulent pericarditis.

15. Dillingham: The left pleura contained some large blood clots whose source was not found; it was lined with pyogenic membrane. There was an adherent pericardium.

16. Broadbent: Obliterative pericarditis. The pericardium was adherent to the central tendon of the diaphragm and to the chest wall.

17. Pel: The heart was displaced slightly to the right. The pericardium was thickened and adherent. There were two encapsulated empyemas, one at the left border of the heart.

18. Cammareri: The parietal pleura was thickened; there was erosion of the ribs in several places; the lung was separated from the cavity by a false membrane; the left side of the mediastinum was thickened; and the left part of the thorax was larger than the right.

19. Light: There was left empyema; the left lung was collapsed; there was acute pleurisy of the right side and acute peritonitis. The heart was in its normal position.

20. Light: There was left empyema; extrapleural abscess communicating with the empyema by a fistula; the left pleura was thickened and adherent to the pericardium; the left lung was collapsed; the heart was twisted, and the pericardium contained eight ounces of clear fluid.

21. Fuchs: There was pyopneumothorax on the left side; the left lung was collapsed and partly adherent to the diaphragm; the heart and aorta were displaced to the right, and a subphrenic abscess communicated with the pleural cavity.

The most notable facts are: that the pericardium was involved in 8 cases, the left lung collapsed in 11 cases, the ribs were eroded in 3 cases, and the pleura perforated in 6 cases.

It is somewhat difficult to classify the cases into those in which pulsation is more or less diffuse without distinct evidence of tumor formation, and those in which tumors actually occur. In many cases the pulsating area is localized, although there may be no local bulging, and sometimes not sufficient distinction has been made between this form and circumscribed pulsation in a projection. As nearly as I have been able to determine there are 50 cases in which definite tumors have been recorded. Of these, 41 cases had a single tumor, 6 cases had 2 tumors, and 3 cases (Henry, Chvostek, and Toft) 3 tumors. Of these cases 37 were apparently empyemas of necessity, although some of them may have been encapsulated pleural abscesses; 11 were abscesses in some part of the thorax, either encapsulated empyemas or pleurisies, mediastinal abscesses, or extrapleural or periosteal abscesses, and 2 (Cruveilhier and Kuhlman) seem to have been cases of serous effusion with distinct local bulging or pointing. Altogether the locality of 62 tumors has been more or less definitely mentioned. Of these, 3 were situated on the right side and 58 on the left side. The 4 tumors situated on the right side were distributed as follows: in the second interspace at right border of sternum (Heyfelder); from second to fifth ribs, right border of sternum (Reyher); seventh interspace, right

border of sternum (Wilks). Of those on the left side, 2 were not localized very accurately; were on the anterior aspect of the chest; in the axillary area, and 10 posteriorly. Of the 42 in the anterior aspect, one (Cruveilhier) had a conoid tumor presenting in front of the sternum; one (Vidal) a mediastinal abscess that had perforated the lower portion of the sternum just to the left; 2 (McCosh, Martin) below the left clavicle; 4 (Plagge, Muller, Light, Wilson) were rather extensive tumors of the left side of the chest, usually discolored and reducible; 19 occupied the various interspaces from the second to the eighth, often more than one, just to the left of the sternum. In one case (Toft) 3 tumors were found at different levels in this situation; 14 were found in the precordial region; 10 tumors in the posterior portion of the chest, of which 4 were below the angle of the scapula, and 4 between the crest of the ilium and the lower border of the ribs just to the left of the spinal column; 1 was in the tenth interspace to the left of the spinal column, and 1 was not distinctly located.

It appears from this analysis that the commonest situation is beneath the costal cartilages on either side of the sternum, 22 tumors having occurred in this situation. Fourteen tumors were in the precordial region; 4 beneath the angle of the scapula on the left side, and 4 wholly below the ribs in the left lumbar region. The other tumors were somewhat irregularly distributed, probably as a result of purely local conditions. The 2 tumors that occurred in association with serous effusion had unusual situations in front of the sternum and in the left hypochondrium.

Of the cases without tumor formation, 2 occurred on the right side (Keppler, Borgiotti). In Keppler's case there were 2 encapsulated pleural effusions which gave rise to diffuse pulsation of the lateral and anterior aspects of the chest. After these were evacuated the pulsation ceased in spite of the accumulation of pus later. In Borgiotti's case there was pyopneumothorax on the right side, and the whole of the right side of the chest was involved in the pulsation. Diffuse expansile pulsation was noted in 5 cases of empyema (Stokes, Béclère, Toft, Dillingham, and Rummel), and in 3 cases of pyopneumothorax (Féréol, Wilson, and Sallés). In 2 cases (Roux and Salles) the pulsation is said to have been diffuse, but its extent is not given. In 4 cases (Flint, Bimmerman, Pitorelli, and Proust) it is not distinctly localized. The pulsation is localized as follows: in the axillary region, 6 cases; in the posterior inferior aspect of the chest, 4 cases; in the anterior region either near the sternum, in the subclavicular, or in the mammary region, 6 cases. In the case of McPhedran pulsation was seen in the axilla if the patient lay upon her back, and in the back if she lay on the right side.

In 3 cases of serous pleurisy more or less localized pulsation was seen as follows: from the sternum to the left of the axillary line, and from the clavicle to the fourth rib (Osler); in the lower

aspect of the left chest (Bailey) and in the left hypochondrium back of the false ribs (Lepine). The limited diffuse pulsation is seen in a much larger proportion of the cases in the axillary and lower posterior regions than is the circumscribed tumor.

Two of the cases (Martinez and Sailer) were hæmothorax. In the case of McPhedran the fluid on the first aspiration was bloody, but subsequently became clear. In the case of Dillingham there was apparently distinct empyema, but at the autopsy large blood clots were found in the pleural cavity. In the case of Innocenti and Marsili blood was also found in the pleural cavity upon aspiration. This patient had tuberculosis.

Martinez's patient was a man, aged twenty-one years, who had cough, pain in the left chest, and gradual progressive weakness. There was diffuse pulsation of the left side of the thorax, involving the epigastrium, more pronounced in the lower than in the upper portion, and a localized pulsation in the second, third, and fourth interspaces between the sternum and the left nipple line. There were all the usual signs of fluid in the left pleura, the heart was dislocated to the right, and its pulsations could be seen and felt in the second, third, and fourth interspaces between the right border of the sternum and the right axillary line. The spleen was low and quite palpable. An operation was performed, and 1500 c.c. of a serosanguinolent fluid was obtained. The heart returned to the left side, the pulsation ceased, and the patient appeared to have recovered.

Two months later he returned with the same symptoms; in a short time carcinoma of the lymph glands developed, and he died. The left thorax was 3½ cm. larger than the right.

The second case I observed at the Philadelphia Hospital. G. B., a West Indian negro, aged thirty years, and a laborer by occupation, was admitted, October 14, 1902. His family history was negative or unknown. He had rheumatism ten years ago; had indulged in alcohol moderately, and in tobacco to excess. For the past year he had suffered from dyspnœa on exertion, palpitation, and, for a time, cough. Three weeks before admission the cough had ceased, but he had suffered from intermittent sharp pain in or around the region of the heart. This became so severe that he was obliged to give up work, and finally entered the hospital. On the day of admission there was a loud systolic murmur heard over the heart, the whole chest, and transmitted loudly into the neck. There was a friction sound synchronous with the heart in the second interspace, just to the right of the sternum; the respiratory murmur over both lungs was normal. The following day the percussion note over the left thorax was found to be absolutely flat. Tactile fremitus and vocal resonance were absent; the breath sounds could not be heard. Over the whole of the left chest a very loud rasping systolic murmur was audible. There was distinct pulsation of the

whole of the left side. On the following day (the 16th) I dictated the following notes:

The patient is slender and muscular; the skeleton is normal; the mucous membranes are pale. The pupils are normal and react to light; there is systolic expansile pulsation in the neck and in the suprasternal notch. There is heaving impulse over the upper portion of the left thorax, extending as far as the posterior axillary line. The maximum impulse is in the fifth interspace in the nipple line. There is distinct impulse in the sixth interspace one inch outside the nipple line. Pulsation can be seen and felt as far as the tenth interspace in the posterior axillary line, and is distinctly expansile in time. There is pulsation of the upper portion of the abdomen synchronous with the heart, and a vigorous downward pulsation in the left hypochondrium. There is systolic impulse in the neck visible in the suprasternal notch. Over the apex there is a faint systolic thrill and a diastolic shock. In the second interspace to the right of the sternum there is a faint systolic thrill and a diastolic shock. In the second interspace to the left there is a powerful heaving systolic impulse, a strong diastolic shock, and an almost imperceptible thrill. Toward the axilla the thrill becomes fainter, and the systolic impulse is very powerful. In the third and fourth interspaces the systolic and especially the diastolic impulses are strong and the thrill is very faint. The systolic impulse can be felt as far as the costal border, and merges into the powerful hypochondrial pulsation. There is no pulsation at the umbilicus. There is slight pulsation in the right hypochondrium from the median to the nipple line. The radial pulses are equal, small, and rhythmical. The liver dulness commences at the seventh rib and moves with the respiration. There is some dulness on the right side as far as the left border of the sternum. From the clavicle to the border of the ribs there is absolute flatness of the left side anteriorly. The whole left side of the chest is tender, especially in the neighborhood of the fourth and fifth ribs from the nipple to the axillary line. On the right side tactile fremitus is diminished, vocal resonance is lost, respirations are vesicular, expiration is faint. On the left side the breath sounds are entirely absent. Over both lungs anteriorly as well as posteriorly there is a harsh systolic murmur not accompanied by sounds, which is loudest over the left lung posteriorly, and faintest over the right lung posteriorly near the apex. In the sixth interspace the first sound is loud, the second is loud and booming, and there is a faint systolic murmur. From time to time a distinct splashing sound is also heard. In the fifth interspace the first sound is less distinct, there is a long, harsh, systolic murmur, and a moderately accentuated second sound. In the fourth interspace the first sound is fainter, the murmur is harsher, and the second sound more accentuated. In the third interspace the murmur is still harsher, the second sound somewhat fainter, and distinctly

reduplicated. At the pulmonic cartilage a loud, harsh murmur almost drowns the other sounds. The second sound is distinctly reduplicated. On the right side of the sternum the systolic murmur is fainter, and the sounds are almost inaudible. The murmur becomes harsher toward the fifth interspace to the right. On the left side of the sternum the murmur is harsher above, but at the fifth interspace it is faint, and two loud sounds are heard. In the epigastrium a faint first and an accentuated second sound are heard. In the carotids there is a loud, harsh, systolic murmur. In the femoral arteries there are no notes, and only a faint systolic murmur is developed on pressure. *When the patient lies upon the right side the position of the right border of dulness is not changed.* The respirations are labored; expansion on the left side is diminished. The superficial lymph glands are not enlarged. The temperature is normal, and has been so since admission. The respirations vary between 20 and 30, the pulse averages 104. The urine shows traces of albumin, the specific gravity is 1010; there are no casts. The blood pressure with Oliver's tonometer is 130.

On October 17th, with the assistance of the resident physician, Dr. Holmes, I made an exploratory puncture and withdrew pure blood. Aspiration was therefore not performed. The condition of the patient now remained practically unchanged. He was evidently suffering; there was distinct expansile pulsation over the whole left thorax easily elicited by placing one hand in front and the other in the back. The pulsation in the left hypochondrium was about as forceful as the day before.

The diagnosis appeared somewhat obscure. The sudden development of the hæmothorax made a rupture of an aneurysm most likely, and this diagnosis was strengthened by the physical signs, especially the loud murmur heard all over the chest. It seemed difficult, however, to explain why there had been no displacement of the heart to the right. An *x*-ray picture was taken by Dr. G. E. Pfahler, which confirmed the physical diagnosis in so far as it showed dense blackness of the whole of the left side of the thorax, and no dislocation of the heart to the right. The patient died rather suddenly on the morning of October 18th, and at 2 P.M. of the same day Dr. Ellis performed the autopsy. The notes are as follows:

Autopsy. The body of a well-developed male negro. The external examination shows bulging of the left side of the chest that extends from the clavicle to a point about 2 cm. below the nipple, and from the left border of the sternum to the anterior axillary line. In the centre this area is raised approximately 2 cm. higher than the corresponding point on the opposite side. Reflexion of the superficial tissues shows that it is due to a prominence of the ribs and dilatation of the intercostal spaces. On the right side the diaphragm is at the lower border of the fifth rib; on the left it is convex downward, the lower portion reaching the lower border of the

rib. There are old firm adhesions between the omentum, spleen, and diaphragm, and between the spleen and left lobe of the liver. The right pleural cavity is normal. The left contains about three litres of blood, about two-thirds of which is clotted, the clots being perfectly free in the cavity. Extending toward the left from a point corresponding to the left midclavicular line there is a fairly formed band of adhesions, 8 cm. long, between the pleura, covering the second and third ribs, and what is apparently a dilated portion of the aorta. The left lung is compressed backward and to the right; it is about the size of a fist, and entirely atelectatic. The long axis of the heart is more transverse than normal. The heart extends about 5 cm. to the left and 5 cm. to the right of the median line. The pericardium is almost universally adherent by fibrinous attachments which can be broken. Aside from a slight thickening of the mitral and tricuspid leaflets, the interior of the heart is normal. Three cm. from the aortic valves there is an opening 6 cm. in length in the posterior superior portion of the aorta which communicates with a sac which extends upward and to the left. The sac projects a distance of 12 cm. from the aorta; the transverse diameter is about 12 cm. At a distance of about 5 cm. from the aorta there is an irregular slit-like opening 1 cm. in length, and there is also a second opening 3 cm. from this ½ cm. in length. The interior of the sac contains several large areas of adherent laminated blood clots; the aorta contains a few atheromatous patches just below the valves. The organs of the abdomen show nothing of interest. The pathological diagnosis is ruptured aneurysm of the ascending and transverse portions of the arch of the aorta, atheroma of the aorta, atelectasis of the left lung, and left hæmothorax.

The actual mechanism by which these diffuse localized pulsations of the thoracic wall are produced has been the subject of some dispute. Unquestionably a number of factors are active, and confusion is due rather to the fact that stress has been laid upon different ones by different investigators than that there is much actual difference of opinion. The source of the pulsation must be the heart or the great vessels. The majority of writers consider the heart the source. The pulsation must be transmitted through the pericardium, the pleura, possibly through the lung, and through the fluid or air, or both, in the pleural cavity to the point at which it is manifested. For practical purposes the thorax may be considered to be a box closed at the sides and above by a bony framework which is somewhat more yielding on either side of the sternum and on either side of the spinal column near its lower border. Below it is closed by a muscular membrane which is always in a state of tension as a result of the elasticity of the lung. This box is divided by a vertical partition composed of two layers of the parietal pleura on the right and left sides, and between them the heart in its pericardial sac, the great vessels arising from its base, the trachea, the

œsophagus, the nerves, minor bloodvessels, and glands of the mediastinal space. Under ordinary conditions the pulsations of the heart, with the exception of the apex, are entirely absorbed by the lungs, always in a state of negative pressure. It has been shown (Regnard) that with each pulsation of the heart the lungs contract slightly. If one lung is replaced by fluid under ordinary conditions pulsation will not be transmitted to the wall of the chest, because the pulsation of the heart is absorbed by the remaining lung. In the 3 cases in which I introduced a hollow needle communicating with a manometer, no cardiac pulsation could be observed; the respiratory movement, however, was in both cases considerable. In these cases there was sufficient positive pressure during inspiration to maintain the level of the fluid in a glass tube at the height of the shoulder, and during expiration it rose somewhat higher. In another case that I had examined carefully for palpable or visible pulsation, the moment the trocar was introduced the fluid spurted out with considerable force, indicating a high degree of positive pressure. I, therefore, doubt whether pulsation occurs in all cases of pleural effusion. Comby, who was the first to consider the question in a scientific manner, laid great stress upon the collapse of the lung. He believed that if the lung on the left side still contained air it was impossible for pulsation to be transmitted. In the cases that he analyzed his contention appeared to be supported, there being always actual evidence or reason to believe that the lung was completely collapsed. This, of course, is the usual condition in chronic empyema.

The theories which have been suggested may be classified as follows:

1. It is due chiefly to the violent action of the heart, the impulse being transmitted through the fluid exactly as the wave of fluctuation is transmitted through the fluid in ascites. This theory is held by MacDonnell, Fraentzel, and Wintrich. Le Roy and Aran, two of the earlier observers, seem to regard it as the most likely explanation, although their statements are not very clear. Traube supposes that in addition there must be a pericardial exudate. Keppler, Fuchs, Auerbach, Light, Bouveret, Innocenti and Marsili, and Henry consider violent action of the heart as an essential cause, but not the only one.

2. Those theories which depend upon the assumption of the existence of adhesions so limiting the fluid or bringing it into closer contact with the heart that the pulsations of the latter are more readily imparted to it. Keppler, for example, believes that the exudate must be in part encapsulated, then compressed by the thoracic wall, and brought into intimate association with the vigorously pulsating heart. Gueneau de Mussy and Broadbent lay especial stress upon pericardial adhesions. That these are sufficiently common in cases of pulsating pleural effusion, a considera-

tion of the autopsy records will demonstrate; but they do not appear to be invariably present, and therefore cannot, as Comby remarks, be the sole cause.

3. Several authors have discussed the possibility of a peculiar quality in the liquid. Comby, Toft, and others have supposed that only in cases of empyema did the pulsation exist. The preponderance of such cases lends considerable color to this view, but if the reports of serous and hemorrhagic effusion were not sufficient to disprove it, the ingenious experiment of McCosh, who filled the sac of an empyema with normal sterile salt solution after washing out the pus, and obtained a reproduction of the pulsation, would be sufficient to show that it had no basis in fact. Comby admits in his last publication that the character of the fluid is not of importance. Féréol's belief that there must be an accumulation of air under pressure has very little evidence to support it. In many cases a pneumothorax was not present. In others it certainly occurred after the puncture.

4. The observation that the withdrawal of a part of the fluid usually abolished the pulsation, and at the same time reduced the tension, led to the supposition that it was the intrathoracic tension, or, rather, the positive pressure in the liquid, that caused the pulsation.

This view has been particularly supported by Osler. It is also considered as one of the elements of explanation by Béclère and Bouveret, and meets with the approval of Toft, Henry, Lépine, Auerbach, Light, and, indeed, nearly all clinicians who have observed cases. Undoubtedly there must be a certain degree of pressure, otherwise the pulsation would not exist; but Lépine has observed that the pulsation may become more violent after the withdrawal of a portion of the fluid, or may even appear for the first time in a reaccumulation after one or more evacuations. In Toulmin's case the withdrawal of part of the liquid did not cause the pulsation to disappear, and he was led to doubt the importance of tension. Cases have also been observed in which more than one tumor was present, the pulsation occurring only in that which was most dependent, so that the mere degree of intrathoracic tension could not alone affect it. Walshe, who was one of the earliest to speculate upon this subject, believed that the tension had little to do with it, and that the pulsation was merely a manifestation of ability to transmit shocks normally found in all liquids.

5. A fifth group of explanations insist chiefly upon the fixation of the walls of the space that contains the pleural exudate. This, of course, comprises the diaphragm, mediastinum, and ribs. Destole believes that there must be immobilization of the diaphragm, partly as a result of the pressure of the pleural fluid which in time equalizes its contractile force and compresses it downward until it becomes comparable to an inert elastic membrane projecting into

the abdomen, partly by the formation of a tense false membrane upon the parietal layer of the pleura.

6. Akin to this, but expressed in a somewhat different manner, is the theory that the pulsation is manifested when the tension of the mediastinum and diaphragm becomes greater than that of the chest wall. Light gives the following explanation: the resistance of the diaphragm, mediastinum, and lung must be augmented until it becomes greater than that of the intercostal spaces. This may be produced either if the effusion is very great, or if there is a thick membrane lining the pleura. Bouveret regards the increase in the resistance of the diaphragm and mediastinum as essential to the occurrence of pulsation. Béclère believes that he has proven by experiments upon the cadaver by means of the Roentgen rays, and by means of observations upon a patient with a funnel-shaped chest, that unless the resistance of a fibrinous mediastinitis is greater than that of the intercostal spaces, pulsation is not manifest. Auerbach agrees with him, and suggests that the fact that pulsation of the heart is more vigorous on the left than on the right side explains why pulsation is more common in cases of left-sided pleurisies. In all of Toft's cases fixation of the mediastinum was favored by obstruction to the dislocation of the heart. Essentially the same idea is expressed by those who believe that the weakening of the resistance of the wall of the thorax is the most important factor. Strongly in favor of this view is, of course, the fact that pulsation anteriorly is so common beneath the weak cartilaginous portion of the ribs, and posteriorly in the neighborhood of the floating ribs. Comby mentioned the dilatation of the intercostal spaces and the paralysis of the intercostal muscles as a contributing but not an essential cause. Rummo, however, considers it of considerable importance. Light urges the importance of lessened resistance in determining the position of the pulsation, and Innocenti and Marsili regard the weakening of the chest walls as essential, and McCosh agrees with them, stating that necrosis of the ribs very commonly occurs.

7. The explanation of Wilson differs essentially from that of other investigators. He believes that "there may be (*a*) strands of atelectatic lung tissue reaching from pleural and pericardial adhesions at one extremity, by way of pleural adhesions at the other, to the surface of the chest, and thus acting as conductors of the cardiac impulse; and (*b*) the elasticity of that part of the wall of the thoracic cavity on the left side formed by the diaphragm in its relation to the fundus of the stomach is increased. The latter conditions, together with the convexity of the left wall of the heart in systolic tension, and the almost synchronous diastolic tension of the aorta of the left side of the chest, serve to explain the greater frequency of pulsation in left-sided effusion." It is conceivable that the systolic retraction might be produced by the adhesion of a sclerotic lung both to the chest wall and to the pericardium, but the results

of autopsies (the only case in favor of Wilson's theory is that of Lorenzutti) and the fact that in the great majority of cases the lung is not found adherent at the point of greatest pulsation, serve to indicate the incorrectness of this view.

The views of those who have studied the subject most carefully regarding the combination of causative factors may be briefly expressed as follows:

Toft: (1) A completely filled pleural sac; (2) dislocation of the heart; (3) involvement of the left side. Pulsation in part may be transmitted by the ascending aorta.

Traube: (1) Pulsation of the left heart; (2) weakening of the thoracic walls; (3) pericardial exudate.

Light: (1) Pressure of the empyema upon the heart; (2) vigorous heart action; (3) a certain degree of tension of the liquid; (4) an area of lessened resistance or increased tension of the mediastinum and diaphragm. Total atelectasis of the lung is not necessary.

Lépine: (1) Compressed lung; (2) diaphragm depressed and tense, but not ad maximum; (3) displacement of the heart to the right; (4) rigidity of the mediastinum.

Innocenti and Marsili: (1) Diminished resistance of the thoracic wall; (2) dislocation and violently acting heart; (3) a thickened pleura.

Béclère: (1) Left-sided effusion; (2) thickening and greater resistance of the mediastinum; (3) lessened resistance of the chest wall.

Comby: Excludes (1) alteration of the heart and bloodvessels; (2) pericarditis; (3) any peculiar character of the liquid. The chief cause is a collapsed lung. Dilatation of the intercostal spaces and muscles favors pulsation.

Fuchs: (1) Energetic heart action; (2) diminished resistance of the wall.

Auerbach: (1) The tension of the mediastinum must be greater than that of the chest wall; (2) the position of the heart toward the left favors pulsation of the left side.

Henry: (1) Left-sided large effusion; (2) relaxation of the thoracic wall from paresis of the intercostal muscles; (3) forcible heart beat.

In the case of pulsating hæmothorax that I report the obliterative pericarditis favored the increased tension of the mediastinum. The large portion of the chest wall with which the fluid was in contact served to increase the amplitude of the pulsation. With each systole of the heart it is evident that a certain amount of fluid was pumped into the chest, increasing also the amplitude of the pulsation, and that at each diastole of the heart the tension in the pleural cavity was sufficient to return a portion to the aneurysmal sac.

Pulsation appears therefore to have been due partly to the fact

that the mediastinal tension was as great as that of the thoracic wall, partly to the simple pumping of fluid into the pleural cavity. Of course, the latter factor could only occur in case of ruptured aneurysm causing a hæmothorax; that in some respects would be considered a false aneurysmal sac. With the majority of those who have studied this subject, I believe that several factors are involved, but also that some of these factors are of more importance than others. The character of the fluid being of no significance, the cause must be sought in the containing walls. If there was no resistance to the continued increase in the quantity of fluid it would soon occupy the entire thoracic cavity. This resistance is found in the mediastinal tissues, which can be stretched only to a limited extent, and this stretching may be further diminished by thickening of the pleura and by pericardial and extrapericardial adhesions. The side of the mediastinum farthest away from the collection of fluid will, as a result of its greater convexity, be tensest, and, therefore, will resist the pulsation of the heart in that direction. Either as a result of depression until it becomes convex downward, when muscular contraction would tend to keep it rigid, or as a result of adhesions in the lower portion of the pleural cavity, the diaphragm also ceases to yield, and the quantity of fluid tends to remain constant. At this stage the resistance of the mediastinum, the diaphragm, and the thoracic walls must, of course, be equal, according to the physical laws of fluid under pressure in confined spaces. If then, pulsation is communicated to this fluid at any one point it will be manifested probably most distinctly at the point diametrically opposite in the containing wall. This pulsation, however, may be modified in a variety of ways. Thus, if the wall at this point is rigid and in some adjacent place is relaxed and weakened, it will be most pronounced in the relaxed portion, and it may occur that, as a result of the local yielding at this point, it will be cumulative. As long as a partly inflated lung is found in the pleural cavity, whose surface is not rendered rigid by thickened pleuræ, it will form a point of lessened resistance and absorb part or all of the pulsation. Therefore, the conditions necessary for the production of the pulsating pleurisy are: first, an accumulation of fluid under such a degree of positive pressure that the pressure upon the wall of the thorax, the mediastinum, and the diaphragm is equalized. Second, the lung must be solid or surrounded by a dense fibrous capsule, or walled off partly by the thickened pleura, partly by adhesions to the chest. Third, the existence of some local point of weakened resistance such as is produced by the empyema necessitatis, or of such a degree of elasticity of the entire thoracic wall that it pulsates as a whole. It is obvious that a thickened parietal pleura which would serve to enhance the other factors might so diminish this that pulsation would not occur.

Two other forms of pulsation occurring in the thoracic walls

are of historical interest. In 1837 Stokes[1] reported a case of pulmonary carcinoma in a man, aged forty-five years, in which there was diastolic double pulsation in the upper sternal and subclavicular regions, accompanied by a bellows murmur. At the autopsy an encephaloid carcinoma of the left upper lobe was found. Graves,[2] in a case of croupous pneumonia of the right side, observed pulsation of the whole of the anterior wall of the thorax quite as vigorous as in the neighborhood of the heart. In this case, also, a bellows murmur was heard over the heart. As far as I have been able to ascertain no cases of either condition have ever been reported subsequently. Both Comby and West speak of them as practically unknown in France and England at the present time. The ability of Stokes and Graves is too great for us to question their powers of observation or diagnosis; but there can be no doubt that such cases are so excessively rare that they need hardly be considered.

The subject may be summarized as follows: Pulsation of the wall of the thorax may be due to disease of the heart or bloodvessels; may be idiopathic, that is, not the result of any definite cause; may be due to pleural or pericardial adhesions; to accumulation of fluid in the pleural cavity, or to abscess of the wall of the thorax. When the pulsation occurs as a result of accumulation of fluid in the pleura the left side is affected in the majority of cases. The patients are usually males and less than forty years of age. The mechanism depends in all probability upon the existence of a positive pressure in the pleural cavity with tension of the mediastinum.

PYOPERICARDIUM AND COMMENCING INTERSTITIAL PNEUMONIA COMPLICATING ILEOCOLITIS IN AN INFANT AGED FOUR AND A HALF MONTHS.

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AND

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Purulent pericarditis is always a secondary affection in infancy and early childhood, and is prevalent in inverse proportion to the age of the patient. Thus of 66 cases of pericarditis seen by Baginsky under fourteen years of age, 20 were purulent, and of these 11 were in the first year of life, the oldest being seven years. Monti saw, among 35 pericarditides in children, 5 in sucklings, all of which

[1] A Treatise on the Diagnosis and Treatment of the Diseases of the Chest, London, 1882, Part I., p. 391.

[2] Ibid., p. 292.

were suppurative. Batten observed 6 purulent cases under three years, 1 of which was four, 1 ten, and 1 eighteen months old; and Still, in 67 pericarditides of non-rheumatic origin, discovered 17 in which the fluid was slightly turbid, with a few flakes of lymph, and 11 in which pus was actually present. Of the first group, 12 occurred within the first three years, while all of the 11 pus cases were under three years; so that 23 of the 28 cases were within the third year of life.

It would appear, therefore, that effusion into the pericardium is almost always purulent in infancy and early childhood, and in the newborn is invariably so, being usually the result of infection through the navel, although there may be other ports of entry.

After the first month suppurative pericarditis is less frequently encountered, but from the middle of the first year it is again met with, decreasing in frequency up to the fifth or sixth year, when the influence of rheumatism comes into play; the pericarditis of which, being, as a rule, serous, does not concern us at this time. When we inquire into the frequency with which purulent effusion into the pericardium occurs in early life we must conclude that it is probably more prevalent than is generally supposed. Because of the great difficulty in recognizing the condition, the diagnosis, in infants, at least, is usually, as in our case, first made at the autopsy-table (Coutts, Batten, Baginsky). Batten, for instance, found it present in 3 per cent. of the autopsies in the Great Ormond Street Hospital for Children; and Still, in about the same proportion, viz., 28 cases in 769 autopsies upon children (3.6 per cent.). In 364 autopsies at the Children's Hospital, Philadelphia, the percentage of cases in which actual pus was present in the pericardium was 1.1 per cent., and of cases in which the fluid was slightly turbid, with flakes of lymph, 1.1 per cent., a combined percentage of 2.2 per cent. of cases which may justly be regarded as purulent.

In the first month suppurative pericarditis occurs as part of the septic processes, so common in the newborn; later in infancy and in early childhood it may owe its origin to a variety of affections. Thus pleurisy and empyema, pneumonia, tuberculosis (usually of adjacent organs), the acute infectious diseases, follicular angina, otitis and mastoid disease, gastroenteritis, osteomyelitis and bone caries, chronic nephritis, gastric ulcer, affections of the mediastinum, peritonitis, meningitis, abscesses of the skin, and other pyogenic processes have all been found associated with purulent pericarditis. Its connection with enteritis, without an intervening pneumonia, mentioned by C. Gerhardt and Baginsky, are the only instances we are aware of, except our own case, in which the primary affection was in the intestinal canal. According to Still, the most common cause is pneumonia, especially pleurisy and empyema complicating pneumonia. This occurred in 22 of his 23 cases of purulent pericarditis under three years; of the whole 28 pyopericardii observed by

this writer, 24 were associated with empyema. In the Children's Hospital the proportion is much lower, only 50 per cent. of the cases being associated with pneumonia or pleurisy.

As to the bacteria met with in suppurative pericarditis, the pneumococcus appears to be the most frequent; indeed, Still and Coutts, from a study of their cases, conclude that it is almost invariably the offending micro-organism. The species of bacteria present in a given case is usually that of the primary affection: in the septic forms the streptococcus or staphylococcus; in tubercular pericarditis the tubercle bacillus; in cases following pneumonia the pneumococcus; occasionally the Friedländer bacillus has been found; one of Baginsky's cases was due to the pyocyaneus, and another to the colon bacillus. The pericardium may be infected at a very early stage of the primary disease, or at a later period, or as a terminal event, as was probably the case in our patient.

Owing to the insidious onset, indefinite symptoms and the paucity and uncertain nature of the physical signs, the disease is generally unrecognized during life. The patient may present the appearance of a grave malady; there may be cachexia, restlessness, feeble pulse, and fluctuating temperature. But in the very young all these symptoms may be absent; especially may the patient be quite fever free, or have a subnormal temperature, while all indications of cardiac disease may be missing, and the most certain, in fact, the only positive means for recognizing pericardial effusions, viz., the physical signs, are, according to the testimony of experienced clinicians, notorious for their rarity and indefiniteness. The heart sounds may be dull, and the apex beat weak or absent (signs difficult to appreciate in infants); but friction rubs are seldom if ever heard, and, except in large effusions, the most reliable sign, increase in the cardiac dulness, cannot be demonstrated. This is due to the small amount of pus generally present; to the limiting by adhesions of small collections of pus to the base of the heart; to the frequent presence of left-sided empyema or consolidation; but, above all, to the absence or slight degree of dilatation of the heart, a feature so constantly present in the pericarditides of older children and adults. For these reasons the diagnosis is very apt, as in our case, to come first as a surprise at the autopsy table (Baginsky), and no discredit attaches to the failure to recognize the affection during life.

As the issue is almost invariably fatal in the suppurative pericarditis of infancy, and as in timely drainage lies the only hope of saving life, we should make, in all affections of the young in which pericarditis is likely to supervene, careful daily examinations of the cardiac area. Especially should free drainage be established as early as possible in all cases where turbid serum or lymph are present in the pleural sac, because such presence, as long as it remains, exposes the patient to the risk of pericardial inflammation (Still). The same may be said of pyogenic processes and collections

of pus wherever situated. With these preliminary remarks, we present the history of the patient whose case is the subject of this paper:

Eddie A., a foundling, aged four and a half months, was admitted to the Children's Hospital October 16, 1903. He had been fed entirely upon condensed milk since birth and had gained very slightly in weight. Otherwise the patient had been in fairly good health, with little indigestion or diarrhœa. Five days before admission he "caught cold"—*i. e.*, had fever, coryza, cough, etc. Simultaneously there was a profuse, greenish diarrhœa, with much mucus and blood and some tenesmus. When first seen the patient was having from six to ten stools daily of greenish, bloody mucus; there was great prostration, a temperature ranging but little above normal (99° to 100° F.), a pulse of 140, and a respiration rate of from 32 to 40. The head was retracted and the neck muscles somewhat rigid. A slight internal strabismus of the right eye appeared to be present, and the conjunctival reflex was readily elicited. The knee-jerks were exaggerated, but there was no ankle clonus, nor could Kernig's sign or the Babinski reflex be demonstrated. The infant was rickety and undersized. Subcrepitant rales could be heard at the bases of both lungs, but the percussion note was clear, and there were no signs of pneumonia. During the patient's short life in the hospital the temperature fluctuated widely, with a daily maximum of between 100° to 101° F., falling to normal just before death. The stools were numerous, largely composed of mucus, the blood disappearing as the case progressed. The slight meningeal symptoms above noted, with the exception of the strabismus, persisted; but were attributed rather to toxæmia than to meningitis. Two lumbar punctures were made, but no fluid was obtained. The urine was voided freely and was negative. At no time was there any indication of cardiac implication; the heart sound, it is true, became quite feeble before death, a symptom readily explained by the marked asthenia. The cardiac area, however, was not percussed. During the two weeks the patient was in the hospital there had been a loss of weight of eighteen ounces. Death was due to asthenia.

From the Pathological Laboratory of the Children's Hospital.
Dr. J. C. Gittings.

The following is a brief résumé of the notes taken at the autopsy of Eddie A., performed twenty-two hours after death:

Body of a moderately emaciated white boy. The abdominal organs are normally situated. The intestines are distended with gas. On section the mucosa of the large bowel is thickened, covered with tenacious mucus, moderately congested, and shows numerous enlarged and prominent follicles. There is no ulceration. The liver is fatty. The gall-bladder is distended with dark-brown, highly

viscid bile, which can be forced through the common duct with difficulty. The spleen and kidneys are moderately congested. Both ureters are dilated (5 mm. in diameter), but no obstruction can be found. In other respects the abdominal organs and structures appear normal.

The pericardium is slightly distended. It contains about 15 c.c. of cloudy serofibrinous exudate. Both layers of the pericardium are covered with a rough, "plush-like" layer of fibrin. This is especially marked over the base, at the point of origin of the great vessels. The process is recent, and the heart muscle presents no change. The endocardium is normal.

The right lung weighs 36 grams. The pleural surfaces are normal in appearance. Throughout the middle and lower lobes there is moderate congestion, with here and there small areas of

Chronic interstitial pneumonia: *l*, lung tissue; *c*, broad bands of connective tissue.

consolidation. Sections exude a slight amount of blood-tinged, foamy serum. The bronchial glands are slightly enlarged and deeply congested.

The left lung weighs 29 grams, and shows the same changes, to a less extent. Sections hardened in Müller formol, mounted in paraffin, and stained with hæmatoxylin and eosin show the following:

Liver. Marked congestion, with cloudy swelling of the hepatic cells and areas of fatty degeneration. There is no increase in the connective tissue; the bile ducts appear normal.

Spleen. Moderate congestion; the Malpighian bodies are enlarged and prominent.

Colon. Moderate increase of intertubular tissue, with round-celled infiltration into the submucous tissues. The lymph follicles are large and project into the lumen of the bowel.

Kidney. Granulation of the cells of the convoluted tubules, with exudation into the lumen. The glomeruli are moderately congested. The tubules in the medullary area are filled with granular detritus.

Lungs. Sections from both upper lobes show normal tissue. Sections from the right lower lobe show the following interesting changes: The pleura is greatly thickened and running in from it are numerous broad bands of connective tissue which divide it up into lobules. In some areas the bronchioles are very large and seem to be increased in number. (This is in part explained by the fact that the lung tissue is shrunken and the bronchioles are, therefore, relatively prominent.) The connective tissue around many of the bronchioles is infiltrated with polymorphonuclear cells. Many of the air cells are greatly dilated and distended with a few desquamated lining cells and numerous polymorphonuclear leukocytes. The alveolar walls in many places are thickened. In other areas the air cells are filled with polymorphonuclear cells and a few red blood cells. The bronchial lymph glands are congested.

Heart. The pericardium shows on its visceral surface an exudate consisting chiefly of fibrin enclosing polymorphonuclear leukocytes, endothelial cells, and bacteria. Below this fibrinous exudate the loose subendothelial tissue contains numerous congested capillaries, and marked round-celled infiltration. This infiltration extends down between some of the superficial muscle bundles. The muscle fibres show no marked change.

Bacteriology. In sections of the spleen and lung stained with Loeffler's alkaline methylene blue, cocci and diplococci can be seen. These do not stain by Gram's method. They probably represent post-mortem infection. In the heart muscle and the pericardial exudate, cocci, diplococci, and short bacilli are seen. Unfortunately, nothing could be determined from the cultures taken from the pericardial fluid and spleen at autopsy. The original cultures would not grow on reinoculation. They consisted of a mixed growth containing cocci, diplococci, and a short bacillus.

The records of the Children's Hospital contain notes on 364 autopsies performed since September, 1891. Among these cases there was disease of the pericardial sac in 16 (4.39 per cent.). In 4 cases the exudate was described as purulent or fibrinopurulent, in 4 as serofibrinous, and in 2 as fibrinous. Six of the cases showed chronic adhesions without recent exudate. Besides these, there were 19 instances of clear serous exudate in excess of the normal amount (30 c.c. being considered as the normal maximum).

As a "serofibrinous" exudate represents often but an earlier stage of the inflammation, and as the description "cloudy serum containing flakes of lymph" may be interpreted as belonging either to the serofibrinous or purulent classifications, it would seem more rational to consider all exudates as purulent in which the serum was other than clear. From this point of view, 8 of the cases may justly be

regarded as purulent. Confirmatory proof should be furnished by the bacteriological findings, which, we regret, are not available in our own series. As an evidence of the difficulty referred to above, of demonstrating *in vivo* purulent collections in the pericardial sac in infancy and early childhood, we have noted the clinical diagnosis in these cases. In only 2 of them, it will be seen, was the condition recognized during life—*i. e.*, 75 per cent. were not diagnosed.

Case I.—F. S., aged seven years. Clinical diagnosis: Pleurisy with effusion; purulent pericarditis. Pathological diagnosis: Purulent pericarditis; left serofibrinous pleurisy; calcified miliary tubercles in the lungs; purulent arthritis of the knee. Note: The pericardium contained 900 c.c. of fluid. Both the pleurisy and pericarditis were secondary to the infection of the knee.

Case II.—D. S., aged four years. Clinical diagnosis: Lobar pneumonia and pleurisy (double); pericardial effusion. Pathological diagnosis: Purulent pericarditis; double lobar pneumonia and pleurisy (with effusion). Note: The pericardium was "greatly distended."

Case III.—K. D., aged fourteen months. Clinical diagnosis: Pneumonia. Pathological diagnosis: Fibrinopurulent pericarditis; right-sided bronchopneumonia and fibrinopurulent pleurisy. Note: "Large amount" of pericardial fluid.

Case IV.—F. S., aged five years. Clinical diagnosis: Pneumonia. Pathological diagnosis: Fibrinopurulent pericarditis; lobar pneumonia (double); fibrinous pleurisy (left). Note: Amount of pericardial fluid not mentioned.

Cases II., III., and IV. were instances of pericarditis complicating pneumonia.

Case V.—J. B., aged eighteen months. Clinical diagnosis: Bronchopneumonia. Pathological diagnosis: Serofibrinous pericarditis and pleurisy (double). Note: 100 c.c. of pericardial fluid; lungs compressed and almost airless. The pericarditis was secondary to the pleurisy.

Case VI.—B. S., aged three years. Clinical diagnosis: Endocarditis. Pathological diagnosis: Serofibrinous pericarditis; double pleural effusion; hypertrophy and dilatation of the heart; chronic myocarditis. Note: Pericardium distended, displacing the lung. In this case there was a history of a scarlatinal rash five weeks before admission. In other respects the history was indefinite, and it is impossible to decide what was the sequence of events.

Case VII.—A. V., aged eight months. Clinical diagnosis: Organic heart disease. Pathological diagnosis: Serofibrinous pericarditis; chronic mitral and aortic valvulitis; hypertrophy and dilatation of the heart; double pleural effusion; passive congestion of the abdominal organs; infarcts in the lung. Note: "Much" fluid in the pericardial sac. Pericardium presented "bread-and-butter" appearance.

Case VIII.—Aged four and a half months, reported in this paper.

Fifty per cent. of the cases were secondary to pneumonia or pleurisy, which adds further evidence of the importance of these diseases in the etiology of purulent pericarditis. Four of the children were under eighteen months and 6 under four years, thus bearing out the universal testimony that the pericarditis of early life is usually purulent.

Of particular interest was the condition in the lower lobe of the right lung. Jacobi has called attention to the comparative frequency of a pure, proliferative, interstitial, chronic inflammation of the lung. This condition has been included by most authors under the general term fibroid phthisis, or has been considered a distinct sequel to the other inflammatory lung diseases, particularly bronchopneumonia. Jacobi recognizes it as a distinct clinicopathological entity—a primary lung affection—and considers that "it is particularly in infancy and childhood that this class of hypertrophy of the connective tissue, terminating in shrinking, is most frequently, almost exclusively, observed."

In our own case there was no evidence of syphilis; there was no history of pneumonia; alcohol and lead could not have been operative in its causation, and the case, therefore, seems to belong to the class of primary pleurogenic interstitial pneumonias, the etiology of which remains to be determined.

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THE TREATMENT OF CHRONIC INTERNAL HYDROCEPHALUS BY AUTODRAINAGE.

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Internal hydrocephalus was recognized by the ancients, and the hopeless progress of the disease, in spite of medical care, led Hippocrates to tap the distended ventricles.

[1] Read before the Surgical Section of the New York Academy of Medicine, February 5, 1904.

Since his time there have been many and varied attempts to relieve or cure the condition.

Congenital hydrocephalus is usually rapidly fatal after birth, and therefore will not be considered surgically. Acquired hydrocephalus appears several months after birth and progresses rapidly or slowly, steadily or intermittently, or may, in a small number of cases, come to a permanent standstill. There is no spontaneous retrogression.

In the cases examined post-mortem there have been found, almost constantly, inflammatory changes in the choroid plexuses of the ventricles and in the ependyma covering the optic thalami, creating obstruction to the outflow of blood through the venæ Galeni and therefore favoring an abnormal amount of secretion into the ventricles. There is also a more or less extensive general ependymitis, which retards absorption and favors increased secretion into the ventricles.

Another constant and very important lesion is the occlusion of the natural outlet for the ventricular fluid. In very rare cases one or other foramen of Munro may be occluded, causing unilateral hydrocephalus. More commonly either the aqueduct of Sylvius or the foramen of Majendie is closed. Only very rarely is the central canal of the cord involved. These various lesions often result from the extension of a basilar meningitis secondary to traumatism, or tubercular, gastrointestinal, nasal, or other infection.

There is present then a condition due to increased secretion and diminished absorption or escape of the ventricular fluid. The greater the pressure of fluid, the greater the interference with absorption, since the brain is distended, compressed, and its circulation materially retarded. This vicious circle is established early in the disease.

The surgical aim is largely a mechanical one, to allow the escape of the retained fluid so as to save the brain from pressure damage and to favor its return toward normal condition.

The early attempts at surgical relief consisted in simple puncture, with evacuation of more or less of the ventricular contents. This operation was repeated as often as the distention reappeared, while the child lived. A very few cases of improvement or cure have been recorded after this treatment, but by far the greater number have been unfavorably influenced. Repeated punctures, even where infection is not introduced, cause an inflammatory reaction, with the presence of albumin in the ventricular fluid, and an exacerbation of symptoms. A modification of this method consisted in injecting iodine or other cauterizing solution just after tapping the ventricle (as in hydrocele), with the hope of diminishing the ventricular secretion. Patients showed an undue tendency to die after this injection, and the method was discarded.

For a time attention was turned to puncture of the lumbar cord,

with evacuation of spinal fluid, in the hope of diminishing the cerebral distention, as being a procedure attended with less danger. Quincke worked on a number of cases in this manner, but with unsatisfactory results. The same dangers attend repeated punctures of the cord as were noted in case of the brain. A very few cases of improvement have been recorded. As there is no communication between the retained ventricular fluid and the spinal canal or central canal of the cord, little can be hoped for from this method.

The rapid return of cerebral distention after the simple tapping naturally led up to the idea of establishing continuous drainage, and this was done by passing a drain into the ventricle and leading the other end into a mass of sterile dressings on the outside of the head. It is practically impossible to keep these cases from being infected, and they die from this cause, if death from the too rapid emptying of the ventricle does not forestall the entrance of germs.

In one of Keen's cases a most instructive thing occurred. A small rubber tube was inserted into each lateral ventricle, and after the fluid had escaped rather too freely the patient developed a temperature and convulsions. The ventricles were then distended with warm boric acid solution, and the symptoms disappeared almost immediately. This series of events was repeated once or twice.

From the methods outlined up to this point nothing is to be hoped for, since the constant secretion of ventricular fluid requires permanent drainage, and external drainage cannot be continued indefinitely.

In 1896 Dr. Leonard Hill published a series of observations on the *Physiology and Pathology of the Cerebral Circulation.* He demonstrated that the tension of the cerebrospinal fluid and of the blood in the cerebral veins was normally the same, and that any increased intracranial pressure drove the cerebrospinal fluid into the veins and out of the skull.

Also he noted that fluid thrown into the subdural and subarachnoid spaces was rapidly absorbed.

These observations soon suggested the idea of subdural drainage and in 1898 Sutherland and Cheyne operated on two cases. The incision was made in the left inferior angle of the anterior fontanelle, the dura was opened, and one end of a strand of catgut was passed between brain and dura and the other end was carried into the ventricle by means of a thumb forceps. One case died of bronchopneumonia at the end of three months, and the other was still living at the time of the report (six months). No improvement, mental or physical, was noted in either case.

Mikulicz passed a gold tube into the right ventricle, leaving its outer end in the subcutaneous tissues about 5 cm. from the middle line and vertically above the ear. After three weeks the tube

ceased to drain and was then inserted into the opposite ventricle. The child died in six weeks unbenefited.

In a second case he used a glass-wool drain in the same situation, but made it subdural rather than subcutaneous. In this case the disease appeared to be arrested.

Brewer's operation consists in making an osteoplastic occipital flap, a flap in the dura, elevating the posterior lobe of the cerebrum, and with curved dressing forceps pushing a rubber-tissue drain up into the lateral ventricle of one side. The brain is dropped back and the wounds in the dura and overlying parts are rapidly closed. Of the three cases only one lived six weeks, during which time there was a decrease of three inches in the head's circumference.

Senn published a case in 1903 in which he made a large pocket in the subcutaneous tissues of the temporal region for good lymph drainage, inserted one end of a fenestrated rubber tube into the pocket, and then carried the other into the ventricle, between the temporal and frontal bones. The head diminished considerably in size, but the child died in two weeks.

The very great majority of the cases operated upon have died within a short time of operation.

In the literature it is notable that the cases which drained rapidly were most prone to die, and observers have repeatedly mentioned that rapid emptying of the ventricle is apt to be followed by a high rise of temperature and convulsions. (See Keen's case, previously mentioned.) It has been suggested also that the cerebrospinal fluid is poisonous, and therefore, in internal drainage, should not be poured into the general circulation too rapidly.

A method of drainage, then, to be successful, must be internal, must be slow, and must be prolonged or permanent. It would seem as if a small permanent fistula between the ventricles and the subdural space would most closely resemble normal conditions, and in the hope of attaining that end six cases were operated upon as follows, under general anæsthesia:

An osteoplastic flap about two inches in diameter is turned down, with its hinge over the base of the mastoid and just above the level of the horizontal lateral sinus.

In the lower part of the dura mater thus exposed, a semicircular flap, base downward and about one inch in diameter, is made. Frequently there are one or two distended veins beneath this dural flap, and they should not be damaged, for their walls are so friable that neither clamp nor ligature is of much use, and the bleeding is annoying.

The brain immediately protrudes through this dural window. A slender aspirating needle is passed through the second temporo-sphenoidal convolution (which is the one protruding), inward and slightly upward until it enters the ventricle, when the clear fluid

spurts out and is collected in a sterile tube for bacteriological examination. Only a very small amount should be allowed to escape in this way.

The thickness of the brain tissue is measured by observing the length of needle inserted when the fluid begins to escape.

The drain is now made of No. 2, forty-day chromic catgut. Three loops (six strands), about an inch and three-quarters longer than the thickness of the brain, are bound together by a loose spiral of catgut, starting at one end and stopping so as to leave an inch and a quarter of the loops free. In other words, the drain consists of a shaft of six strands of catgut a half-inch longer than the brain thickness and, spreading from its base, three free loops of gut an inch and a quarter long. Around the shaft of the drain, but not covering its tip, are rolled three layers of cargile membrane. With a long, narrow-bladed thumb forceps the tip of the drain is seized and carried into the ventricle along the tract made by the aspirating needle. The tip projects about one-half inch into the ventricle. The free loops of gut are slipped under the dura between it and the brain surface, in different directions, but chiefly downward toward the great lymph spaces at the base of the brain. A sheet of cargile membrane is slipped between the dura and the catgut loops to prevent adhesions. Usually by this time sufficient ventricular fluid has escaped, so that the brain no longer protrudes through the dural window.

The dura is sutured with catgut, the bone-flap is held in place by three or four chromic catgut sutures, the deeper soft tissues by catgut, and finally the skin with silk. A good-sized sterile dressing is applied with some pressure.

The site just above and behind the ear, with the puncture through the second temporosphenoidal convolution, was chosen because the *body* of the lateral ventricle is drained. Where anomalies of the ventricles exist they most frequently involve one or other of the horns. Afterward, moreover, the escaping fluid leaves the brain in close proximity to the great lymph spaces and venous sinuses at its base—a fact which favors its rapid absorption. The right side of the brain is chosen because, if any irritation of the motor areas occurs, the left side of the body is involved, and more particularly Broca's speech centre is not disturbed, as it lies in the left hemisphere.

The approach to the brain is easy; the brain need not be handled, and is but slightly injured in the insertion of the drain.

Drains passed through the dome of the brain, which is always very thin (as in Mikulicz and Sutherland's cases), would be more liable to displacement or to interference with function, because it is here that the brain undergoes most change in contour as the ventricular contents escape. Again, the drainage is farther away from the great channels of exit.

Drainage through the under surface of the occipital lobe is open to objection because it involves handling of the brain itself, which is thin, soft, and friable.

The forty-day chromic catgut was used as a drain with the hope that before it was dissolved a chronic fistulous communication would have formed between the ventricle and subdural space.

The cargile membrane was wrapped about the shaft of the drain to prevent the soft brain tissue from being crowded in between the strands of the drain and so preventing the escape of the ventricular contents. It was also hoped that it would form a facing to the punctured tract and so facilitate the formation of a chronic fistula.

The free loops of catgut coming from the shaft of the drain were pushed between the dura and brain to lead the escaping fluid beyond the area where adhesions would be apt to form between the brain surface and dural flap.

During the closure of the wound the ventricular fluid escapes rather freely. The first dressing is applied firmly with adhesive plaster to limit the external drainage, but, in spite of this, the dressing is well moistened during the first twenty-four hours. After that there is no further external escape of ventricular fluid.

By this method, with slight modifications in the various cases, the following six patients were operated upon during the last two years, at Randall's Island Hospital:

Case I.—David S., aged five and one-half years, had been an inmate of the idiot ward at Randall's Island for several years. No record was made of his history.

The house staff said his head was increasing slowly in size, but no record of measurements had been kept.

Physical Examination. The trunk and extremities were small and poorly nourished. Motion, both active and passive, was free in all the joints (no contractures or ankyloses). Voluntary motion of the extremities was accompanied by muscular tremor and marked ataxia. The condition of the reflexes was not recorded.

The heart, lungs (except for a few rales over each base), the digestive and urinary apparatus were in good order. The head was enormous, with large frontal, parietal, and occipital bosses. The skull was completely ossified.

The head was so heavy that he could neither sit nor stand, nor even roll the head over when lying down.

The eyes protruded forward and downward, showing the sclera between the upper lid and iris. Marked nystagmus was present.

Mental Condition. He recognized his spoken name with an imbecile smile, and when asked what his name was, could speak it. He knew only the simplest monosyllables. He would shake hands with anyone who approached and spoke his name.

The head measurements were: circumference, 62.5 cm.; bisauricular (meatus to meatus over vertex), 43 cm.; nasion to inion,

41 cm. Temperature ranged between 99° and 100° F.; pulse ranged between 96 and 108; respiration ranged between 20 and 24.

July 10, 1902. Operation done under chloroform anæsthesia. In this case a trephine one and one-half inches in diameter was used, and the button of bone was discarded. When the dura was opened the brain protruded a full half-inch beyond it and did not pulsate (evidences of marked tension). With an aspirating needle enough ventricular fluid was evacuated to bring the brain to the dural level (two and one-half ounces), when the drain was inserted and the wound closed. Time of operation, thirty-five minutes. The wound healed by primary union.

Following operation the temperature rose steadily till at the end of sixty hours it reached 106° F. (pulse, 152; respiration, 38). For the next two days it ranged from 103° to 105° F. From this time the temperature ran an irregular course, with a general tendency toward normal, which it reached at the end of the tenth week after operation. During this time there were sibilant and sonorous rales over both lungs, chiefly at the bases.

For the first six weeks the child was in a condition closely resembling the typhoid state, but after that there was slow, steady, general improvement. A week after operation it was first noticed that all the joints of the left upper and lower extremities were continually held in the flexed position. Daily massage and passive motion corrected this difficulty, so that the extremities were freely moved both actively and passively by the end of the third month.

On the fifteenth day after operation there was so much return of intracerebral pressure as to cause a considerable protrusion of cranial contents at the site of operation. With aseptic precautions one and one-quarter ounces of fluid were removed from the ventricle with a fine aspirating needle. On the thirty-fifth day one and one-half ounces were again removed for the same reason. The fluid was clear and proved to be sterile. After each tapping the volume and strength of the pulse improved, but otherwise there was no noticeable effect. Although a certain degree of protrusion persisted, it was never again tense enough to indicate further tapping. After the third month the protrusion grew distinctly softer and smaller, the eyes receded into their cavities, and the nystagmus disappeared. The drainage was now apparently working efficiently.

There has been no physical improvement worth noticing, although it is now twenty months since operation.

The mental improvement is the feature of interest in this case. With recovery from the three months' illness following the operation he began to recognize the doctors, nurses, and the other patients by name, to tell which way they had gone from the room, to call the children to their meals, to quarrel verbally, and to fight with his hands if the other children came sufficiently close, and to sing simple

songs. He is still unable to sit or stand, or move his head while lying down.

Since the skull was completely ossified, no diminution in its size could be expected.

CASE II.—Daniel Z., aged thirteen months. Admitted to hospital February 2, 1903.

Family History. Negative.

The mother's first child was born dead after a difficult labor. The next two children are alive and well.

Personal History. Daniel was the fourth child, was a breech case, was delivered by a midwife, and suffered a broken leg in the process. He was otherwise normal at birth. He never had convulsions or any serious illness. When he was five months old his parents noticed that his head began to grow rapidly, and this abnormal growth has continued.

Physical Examination. The trunk and extremities are of good size, well nourished, and are perfectly normal. The reflexes are normal. The viscera give no evidence of disease. He cannot sit or stand, because of the unwieldy head. He can roll his head about while lying down. The head is large; the anterior fontanelle is large, bulging, and the brain beneath it very tense and not pulsating. The eyes protrude and show the sclera all around the iris. Moderate nystagmus is present. He has four incisor teeth, two in each jaw. He recognizes his mother, apparently.

January 9, 1903. Head measurements: circumference, 49 cm.; bisauricular, 35.75 cm.; nasion to inion, 32.45 cm.

26*th.* Circumference, 50 cm.; bisauricular, 36.20 cm.; nasion to inion, 34.65 cm.

March 12*th.* Circumference, 59 cm.; bisauricular, 43 cm.; nasion to inion, 40 cm., which means an increase per week: circumference, 1 cm. +; bisauricular, 1 cm. —; nasion to inion, 1 cm. —.

13*th.* The operation was done under chloroform anæsthesia. Everything went smoothly, and the operation was finished in thirty minutes. In this case only a small quantity of fluid (half an ounce) was allowed to escape through the aspirating needle.

The maximum temperature in this case after operation was 103° F. on the second day. It fell rapidly to normal and stayed there. The child was at no time really sick. It took milk with appetite after twelve hours. Recovery was uneventful. The wound united by primary union.

The measurements at various dates were as follows:

March 29, 1903 (sixteenth day). Circumference, 59 cm.; bisauricular, 43 cm.; nasion to inion, 40 cm.; oblique diameter of anterior fontanelle, 9.3 cm. each.

April 9*th* (twenty-seventh day). Circumference, 59 cm.; bisauricular, 43 cm.; nasion to inion, 40 cm.; oblique diameter of anterior fontanelle, 9.3 each.

26th (forty-fourth day). Circumference, 59 cm.; bisauricular, 42 cm.; nasion to inion, 41 cm.; oblique diameter of anterior fontanelle, 9.3 each.

May 10th (fifty-eighth day). Ecchymosis appeared in the scalp above and in front of the operative area.

17th (sixty-fifth day. The head appeared asymmetrical (smaller on the right side). Unfortunately measurements taken were not transferred to the record book and were lost. Nystagmus no longer present.

27th (seventy-fifth day). A subperiosteal hæmatoma three inches in diameter appeared just above the operative field. No cause was known for its appearance, and it disappeared spontaneously but slowly.

June 3d (eighty-second day). Circumference, 55.6 cm.; bisauricular, 40.6 cm.; nasion to inion, 37 cm.

26th (one hundred and fifth day). Circumference, 57 cm.; bisauricular, 41.5 cm.; nasion to inion, 38 cm.

Bony union had not occurred in the osteoplastic flap. The head was noticeably smaller and flattened on the right side (side of operation), and permission to operate on the left side was asked, but the parents refused and took the child home.

On November 22, 1903 (two hundred and fifty-fourth day—eight and one-third months), he was seen at his home. His general condition was good: the eyes were not protruding and looked natural and intelligent. No nystagmus. The anterior fontanelle was slightly retracted and normally pulsating. He was playing in his crib, recognized the other members of the family, could say "Mamma," and took an interest in his surroundings.

The measurements of the head were as follows: circumference, 61 cm.; bisauricular, 44.5 cm.; nasion to inion, 41.5 cm.; oblique diameters of the anterior fontanelle, 8 cm. each.

Bony union had occurred between the skull and osteoplastic flap.

On February 2, 1904 (three hundred and twenty-sixth day—eleventh month), there was still further general improvement. He could almost support the head in the erect position, but made no effort to stand. He was begining to talk. The measurements were: circumference, 61.5 cm.; bisauricular, 44 cm.; nasion to inion, 41 cm.; oblique diameters of anterior fontanelle, 7 x 7 cm.

CASE III.—Bella H., aged six and one-half years.

Family History. Negative.

Personal History. Had convulsions when a baby and soon afterward the head began to grow to abnormal size.

Physical Examination. The trunk and extremities were fairly well developed. The reflexes were much exaggerated, especially on the right side.

The head was very large, 61 cm. in circumference, and completely ossified.

The eyes were divergent and protruding.

The child was imbecile.

July 16, 1903. The operation was done under chloroform anæsthesia, and lasted forty minutes. One ounce of ventricular fluid was removed. During the first seven days the temperature ran between 101° and 104° F.; pulse, 118 to 136; respiration, 24 to 28; then gradually fell to normal on the sixteenth day.

The wound healed by primary union.

There was no change for better or worse, mental or physical, in this case. As the head was completely ossified no change in size was to be expected.

On September 10, 1903 (fifty-sixth day), she died of an attack of gastroenteritis.

CASE IV. Annie E., aged five and one-half years.

Family History. Negative.

Personal History. The child was perfectly well and strong until four years of age, when the parents noticed she could not walk so well as usual. Soon afterward they noticed the head was growing more rapidly than before.

At the time of operation, one and one-half years from the onset, both lower extremities were paralyzed, the mental power was feeble, and the head measured 57 cm. in circumference. It was completely ossified.

July 17, 1903. The operation was done under chloroform anæsthesia. In raising the dural flap from the brain, to which it was slightly adherent, a distended vein was divided. Its walls were so friable that there was annoying delay in stopping the hemorrhage.

The aspirating needle passed through 2 cm. of brain tissue to reach the ventricle. An ounce and a half of the fluid was collected for bacteriological examination. (The fluid was sterile.)

The drain (eight strands of No. 2 gut, *i. e.*, a little larger than usual) was inserted, and the operation completed as before. The patient was returned to bed in good condition. The operation lasted one hour. The intracranial tension was considerable, and drainage was free during the closure of the wound, and for twenty-four hours the dressings were well saturated. Before operation the temperature was 99° F.; pulse, 120; respiration, 22. The morning after operation, temperature, 103.8° F.; pulse, 138; respiration, 30. The evening of the second day the temperature had reached 106.2° F.; pulse, 168; respiration, 38; so it was deemed wise to open the wound. There were no signs of infection. Cultures were taken from the wound area, but proved sterile. The brain was under great tension, and nothing was escaping along the drain; so the needle was passed into the ventricle and two ounces of fluid withdrawn. There was temporary improvement in the general condition, but the patient died a few hours later.

The pathologist reported the fluid of this second tap sterile.

It is to be noted that this operation took much longer, the drain was larger, and the escape of fluid at and immediately after the operation, more free than usual.

CASE V.—Benjamin H., aged four years.

Family History. Negative.

Personal History. Was well till six months old, when he had severe convulsions, followed by pneumonia. After this the head grew noticeably, and the child was less bright.

Physical Examination. The trunk and limbs were fairly well developed. The head was large in proportion to the body and completely ossified.

The child is imbecile.

The measurements in this case were lost.

July 31, 1903. The operation was done under chloroform anæsthesia in forty minutes, and went off smoothly. A half-ounce of the ventricular fluid was withdrawn and sent to the pathologist, who reported it sterile.

The day after operation the temperature reached 102.8° F.; pulse, 154; respiration, 30. On the fourth day the temperature was 99.4; pulse, 144; respiration, 30. The patient looked well and took nourishment with relish.

On the sixth day (temperature, 101.6° F.; pulse, 158; respiration, 28) he became restless and irritable, and late in the day there appeared a thick, purulent discharge from the right auditory canal.

On the eighth day anuria developed, and he passed into coma and died, in spite of efforts to stimulate action of the kidneys.

CASE VI.—Frank R., aged ten months.

Family History. Mother's first child died in twelve weeks. Second and third born dead at seven months. Fourth, fifth, and sixth children are all healthy. The patient is the seventh child.

Personal History. Breast fed. Perfectly well until three months old, when he had an attack of fever, convulsions, vomiting, and diarrhœa. The acute attack lasted one week, but convalescence was very slow. Two months after this acute attack the parents noticed his head was growing rapidly.

For some weeks it was noticed that in the late afternoon he was restless, and not infrequently would become rigid for a few minutes.

He entered the hospital November 6, 1903. On November 15th he developed a severe attack of colitis which lasted several weeks. His convalescence was slow.

Physical Examination. The trunk and extremities were unusually large and well nourished, and could be freely moved, actively and passively. The viscera showed no signs of disease. The reflexes were normal.

The head was very large and tense, especially the anterior half. The anterior fontanelle was wide open, protruding, and was con-

tinuous with the posterior one by a space 2 cm. wide between the parietal bones. He could not hold the head erect, but could roll it from side to side while lying down. The eyes were protruded forward and downward and showed sclera between the upper lid and iris. There was slight nystagmus. Two upper incisors were present.

November 11*th*. Head measurements: circumference, 54.5 cm.; bisauricular, 38.6 cm.; nasion to inion, 38.5 cm.

15*th*. Colitis.

19*th*. Circumference, 54.5 cm.; bisauricular, 38.9 cm.; nasion to inion, 38 cm.

December 5*th*. Digestion again good.

24*th*. Circumference, 55 cm.; bisauricular, 39.5 cm.; nasion to inion, 39 cm.

January 16, 1904. Circumference, 56 cm.; bisauricular, 40.5 cm.; nasion to inion, 39.5 cm.

The operation was done under chloroform anæsthesia. The skull and overlying parts were very thin. In this case, again, one of the veins beneath the dura was damaged and caused annoying bleeding and delay. The brain was under great tension, and was very thin, the needle passing in only 1 cm. when the ventricle was reached. One and one-half ounces of fluid were allowed to escape before the brain receded to the level of the dural opening. In closing the wound after inserting the drain, the dura was sutured, the bone-flap was simply laid back in place without sutures, and the soft parts closed over it.

The whole operation went slowly and very unsatisfactorily. It lasted fifty-five minutes.

During the closure of the wound the ventricular fluid escaped freely, so that at the end of the operation the head, which had been tense, was quite relaxed and the fontanelle depressed. This indicated too rapid escape of the fluid, so a firm dressing was applied and strapping was used to reproduce intracranial tension.

For the first twenty-four hours there was a rather free escape of fluid into the dressings, but the patient was apparently doing well, and took nourishment with relish.

Six hours after operation the temperature reached 102° F.; pulse, 130; respiration, 30. The next morning the temperature was 99° F.; pulse, 130; respiration, 30, but in the evening the temperature reached 103.4° F.; pulse, 130; respiration, 34.

On the second day, temperature, 105.4° F.; pulse, 150; respiration, 46. In the night of the second day there appeared spasmodic twitching of the left upper extremity and face. Third day the twitching was more marked and the temperature reached 106° F.; pulse, 160; respiration, 58.

The dressings were changed, and a few drops of pus exuded from beneath the skin-flap. The wound was opened. The pus seemed

to have come entirely from the superficial tissues, as the dura and brain did not appear to be involved. The wound was cleaned, a 1:10,000 bichloride drain placed under the flap, a wet dressing over the wound, and a light-pressure bandage applied. An ice-cap was applied to the head.

The kidneys were not secreting very actively, so a rectal saline irrigation (temperature, 100° F.) was ordered every six hours. After the first irrigation the urine came freely. The twitchings ceased within an hour; the patient became quiet and took nourishment more readily.

During the following two days the temperature descended to 103° F., there were only occasional twitchings, and there seemed to be slight general improvement. The dressings showed no more pus.

In the early morning hours of January 22d (six days after operation) he was left in apparently good condition by the nurse going off duty. A short time afterward the relieving nurse went to look at him and found him dead.

From the time of operation the exophthalmos and the nystagmus disappeared.

RESULTS: *Mortality:* Cases I. and II. are still living, twenty and eleven months, respectively.

Case III. lived two months and died of acute gastrointestinal disturbance.

Case IV. died about sixty hours after operation, and unquestionably as the result of it.

Case V. had apparently reacted from the operation by the fourth day, then developed otitis media, which drained satisfactorily; then, finally, anuria and death on the eighth day. Death probably would not have occurred at that time had no operation been performed.

Case VI. died suddenly on the sixth day, when he had apparently been slowly recovering from the sharp reaction of the first three days. The wound was infected, but apparently not in the deeper tissues.

The mortality of the operation in these six cases, then, was 50 per cent.

	Age.	Fluid evacuated.	Time of operation.		
Case I	5½ yrs.	2½ oz.	35 min.	Marked reaction.	Recovery.
" II.	13 mos.	½ "	30 "	Slight "	"
" III.	6½ yrs.	1 "	40 "	" "	Operative recovery; died in 2 mos. from intercurrent disease.
" IV.	5½ yrs.	1½ oz.	50 min. (vein wounded).	Marked reaction.	Death in 2 days.
" V.	4 yrs.	½ oz.	40 min.	Mild reaction.	Died 8 days; anuria.
" VI.	10 mos.	1½ "	55 " (vein wounded).	Marked reaction. Infection.	Died in 6 days.

It is a fact worthy of notice that in all the cases where the ventricular fluid was evacuated freely at the time of operation, or during the

first twenty-four hours, there was a sharp reaction, shown by the temperature, pulse, and general condition of the patient. (See Cases I., IV., and VI.)

Cases II., III., and V., on the other hand, showed a comparatively mild reaction.

With all due allowances for variations of the cases in other respects, this fact would argue strongly against producing any sudden change in the hydrostatic condition of the brain. The analogy with the disturbances due to sudden evacuation of old, large, pleuritic and abdominal effusions is close.

That prolonged drainage can be obtained by this method seems demonstrated by Cases I. and II.

In Case I., twenty months after operation, the signs of intracranial pressure are still absent, although the head had been slowly growing up to the time of operation (not proven by recorded figures), and at the operation the brain showed evidence of great ventricular distention.

Case II. is even more positive. For nearly ten weeks preceding operation the recorded measurements showed an average increase of 1 cm. per week in the cranial circumference.

Eleven months after operation the circumference is only 2½ cm. greater than at the time of operation. Meantime the whole child has grown much larger. Moreover, the soft, somewhat retracted fontanelle, the absence of exophthalmos and nystagmus show that there is no undue intracranial pressure.

It is interesting to note that in both cases the drainage became most active about two and one-half to three months after operation.

Case I. is considerably improved mentally, but still remains a hopeless physical combination of a feeble body unable to support or move its enormous head. This brain had been subjected for a number of years to pressure, and this during a period normally devoted to its active development, interference with which means irreparable damage for life.

Case II. is much benefited mentally and physically. It is probable that his body and legs will eventually support his head, in which case he may become a fairly normal child. (His tenement-house surroundings are not, by any means, such as to give him the best opportunity for development.)

From what has preceded it seems fair to deduce the following fundamental principles for the operative treatment of chronic internal hydrocephalus:

1. The only feasible method is some form of internal or auto-drainage.

2. Drainage to be successful must be (*a*) permanent or at least prolonged; (*b*) slow, aiming rather to prevent further distention of the brain than to cause rapid emptying of the ventricles. Drainage

through the aqueduct of Sylvius and foramen of Majendie are naturally slow.

3. Operation must (*a*) be brief, to avoid shock in children; (*b*) involve least necessary traumatism to the brain; (*c*) involve but small escape of ventricular fluid, to avoid sudden change in the hydrostatic condition of the brain.

4. Operation, to attain its best results, must be performed early in the disease, before irreparable damage has been done to the brain structures.

Remarks from the Neurologist's Standpoint, by L. Pierce Clark, M.D.

Undoubtedly the success from operative treatment depends not a little upon the age at which operation is done. Early treatment cannot be too emphatically insisted upon. It should be undertaken as soon as the child is old enough to withstand the operation and before ossification is complete. Anything which prevents the development of the child's brain, particularly for the first three years, is attended with serious consequences. The nerve fibres of the pyramidal system perfect their sheath covering during this period. The perfection of this system goes hand in hand with the function of equilibration and co-ordination. Non-development at this period is serious enough in itself, as the child can never quite recover this handicap, even though the cause be removed; but to this non-development in internal hydrocephalus is added degenerative changes because of pressure. The latter gives rise to positive and distressing symptoms. They may be summarized as (*a*) mental weakness; (*b*) convulsions; (*c*) contractures; (*d*) loss of sight. The mental enfeeblement ranges all the way from mild grades of feeblemindedness to that of more or less complete idiocy. The latter state most frequently obtains. Convulsions occur in these cases on account of pressure, primarily, which culminates in many instances in permanent structural changes in the cerebral cortex. The attacks partake of the same general convulsive characteristics as those seen in idiopathic epilepsy, and the cell change underlying the fit in the two instances are probably identical. Epilepsy in hydrocephalus, however, is never recovered from. Convulsions which increase in frequency and have a tendency to occur in groups or series should in themselves speak for early operation.

The contractures which soon develop in these cases due to destruction in the motor tracts are usually heralded for a time, however, by gradually increasing spasticity, in the lower limbs first and finally in the arms. When this spasticity can be easily overcome by passive movement the disturbance in the motor tracts is not probably beyond that of irritation, and can be recovered from in greater part—a point of considerable value in prognosis in operative treatment.

One of the most distressing symptoms which adds to the climax of bodily helplessness in hydrocephalus is the occurrence of more or less complete blindness. This is caused by one or all three means: (*a*) pressure on the optic thalamus and optic radiation; (*b*) pressure on the optic chiasm; (*c*) traction upon the optic nerve. Inasmuch as total blindness is heralded for some time by paroxysmal temporal hemiopia, pressure on the optic chiasm is probably the main cause of blindness in most instances.

It is just possible that the *x*-ray may yet help us to measure the amount of fluid distention in the ventricles, the thickness of the cerebral cortex, and the state of cranial bones.

There can be no doubt that the success of any operative procedure must embrace (*a*) the minimum of brain manipulation; (*b*) slow and permanent drainage, which conditions, I believe, Dr. Taylor's operation has fairly met. Possibly a slight continuous compression of the head might avoid the too sudden withdrawal of the inhibitory cerebral control over the lower medullary centres, the too sudden withdrawal of which has only too often expressed itself in the past in anuria, convulsions, high temperature, vasomotor and secretory disorders of the abdominal viscera.

The after-treatment of these cases resolves itself into a problem of medicopedagogical training.

It would seem hardly necessary at the present day to speak against the establishment of a profuse diarrhœa, diuresis, or the use of large doses of mercury and iodides to aid drainage in such weakened organisms as hydrocephalic children, were such procedure not still advocated in some text-books.

I have had the opportunity of following four of Dr. Taylor's cases through the operative treatment, and I think he states the results fairly. His operation not only seems the most feasible, but is along the line destined to promise the best results in treatment of a well-nigh hopeless affection if allowed to take its natural morbid course.

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A CASE OF SPLENOMEGALY WITH BLOOD CHANGES AND SYMPTOMS RESEMBLING THOSE OF BANTI'S DISEASE, APPARENTLY DUE TO MALARIA.[1]

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After Osler's[2] careful studies of conditions resembling the one about to be described, and the work of Lippy, Wentworth, and others, cited by him, an historical or pathological discussion to which no new fact could be contributed would be out of place. As the patient whose case I wish to put on record is living and apparently improving, and as the affection with which she suffers is usually chronic, there is no reason to wait for an autopsy (which we are bound to hope will long be postponed) before reporting the clinical observation. Moreover, single cases may be of importance in the final classification of a subject as yet very obscure.

As Osler has pointed out, and as we can all recall as we pass in review our personal observation, either of cases carefully studied and recorded, or of cases vaguely recalled of which no scientific record was made, the combination of enlarged spleen, enlarged liver and blood changes of an anæmic or chlorotic type, is not exceptional, while combinations of two of these three factors are not infrequent. There seems, however, to be among the motley groups in which these pathological factors are commingled in various

[1] Paper read and patient presented before the College of Physicians of Philadelphia, March 2, 1904.

[2] The American Journal of the Medical Sciences, 1900, vol. cxix.; Transactions of the Association of American Physicians, 1902, vol. xvii. pp. 428, 456.

sequence and degree one which may be separated as possessing certain additional characteristic symptoms and of which Lichty[1] in a recent literary study could find record of only 34 cases sufficiently described. To this group of cases Osler would affix and restrict the designation *anæmia splenica*, and even *anæmia splenica chronica*. Of its earliest stages little is, or from its nature is likely to be, known; of its intermediate stages much has been written; and to its late stages the name of Banti's disease has been given. If we accept Osler's definition in its entirety, the case to be reported does not fall within the group he has erected; for he insists on an unknown etiology, especially excluding malaria and syphilis. On the other hand, while there is no diminution of leukocytes, the enormous size of the spleen, the peculiar pigmentation of the skin, the pulmonary, nasal, and gastrointestinal hemorrhages, the apparently secondary character of the hepatic involvement, the diminution of erythrocytes, and the low hæmoglobin content of the blood, tally precisely with Osler's description.

The blood was carefully studied by competent observers without finding parasites until—following the administration of quinine—it was again examined by Dr. Rosenberger, who succeeded in demonstrating an organism of a type not common, at least in the United States. Several interesting diagnostic queries thus arise. In the absence of the discovery of the organism, would the case have come into Osler's group, and is it now to be excluded? Is it possible that in any large number of the recorded cases examination at an earlier stage—for our case is probably of not more than two years' duration—would have revealed malarial parasites? Is it possible that in recorded cases in which the parasite is said to have been absent, and in which no distinct history of malaria was given, administration of a sufficiently active salt of quinine would have driven parasites into the peripheral circulation, where they could have been found? I can have no definite answer to propose to these queries, and I have not studied all the recorded cases with sufficient critical minuteness to hazard a guess. I am satisfied that in very many cases, certainly in those in which Osler reports its absence, malaria was not present. But are we to be restricted entirely to an etiological diagnosis in this obscure condition, as we are properly restricting ourselves wherever possible? Are we at all sure that all the accepted cases have one and the same etiology? If a multiple etiology be permissible, why draw the line at malaria? except it be on the same principle as Dickens' barber, who remarked to a man whom he had declined to shave, that "the line 'ad to be drawn somewhere, and he drew it at coal 'eavers." In Lichty's tables the line is not drawn at the humble plasmodium or even at less respectable germs. He includes 7 cases

[1] Journal of the American Medical Association, February 20, 1904, p. 528. Eshner's case is not included in this list, and probably others might be added.

of malaria and 2 of syphilis. I quote in summary the other features of his analysis. Twenty-six cases were males, 8 females; the average age was thirty-six years. Melanoderma was present in 17 cases. Splenic enlargement was the most prominent feature in all, and anæmia the next. Hemorrhage occurred in 24. Hæmoglobin averaged 47 per cent.; the red cells, 3,293,000; white cells, 5594. Excluding 2 cases in which there was leukocytosis, the leukocytes averaged 4381. The liver was enlarged in 16 cases, small in 1. Ascites was present in 7, swelling of feet and legs in 9, glandular enlargement in 3, gastrointestinal symptoms in 8, and cardiac murmurs, generally hæmic, in 11. In only 2 cases was there albumin, a trace, while the 1 reported by Lichty had considerable at times, as well as pus and casts. Of 25 cases treated medically, only 5 recovered, 12 were improved, and 7 died, hemorrhage having been the commonest cause. Operation was performed in 8 cases, with 5 recoveries and 3 deaths.

I may also note at this point that even in Osler's own series of 18 cases, malaria had been present in 5. Osler excludes it as a factor in the splenic anæmia, however, on the ground of time. In 3 of the patients (aged forty years, fifty-six years, and thirty years) the infection was in childhood; in only 2 was it in adult life—in 1, twelve years, in the other eighteen years before the onset of the present illness. In view of the tendency of the malarial organism to lie dormant for long periods, possibly in the spleen, possibly in the bone-marrow, possibly elsewhere, in an unknown stage, and over many years—more than twenty years in 1 of my cases of chronic, recurrent malaria—can we be sure that this admitted infection was devoid of moment in the cases reported? It is true that in cases of prolonged malarial infection (and such was the fact in the instance I have referred to) paroxysms of various kinds are usually manifested with some kind of periodicity—recurring annually or semi-annually, as a rule—and that well-timed, persistent search in the peripheral blood, especially if the patient be placed under the influence of quinine, iron, or residence at an altitude, will eventually find the organism. Nevertheless, in my case of long-standing malarial infection, there were many successive months when organisms were invisible to almost daily search in the peripheral blood, and others have had similar experience. Thus the possibility of the existence of malarial infection, despite the failure of good observers to discover the organisms, must be admitted; and with this admission, until a definite etiology is established for the anæmia splenica of Osler, cases conforming clinically to the type may usefully be studied together.

Osler's definition is: "A chronic affection, probably an intoxication of unknown origin, characterized by a progressive enlargement of the spleen, which cannot be correlated with any known cause, as malaria, leukæmia, syphilis, cirrhosis of the liver, etc. (primary

splenomegaly); anæmia of a secondary or chlorotic type (leukopenia), a marked tendency to hemorrhage, particularly from the stomach, and in many cases a terminal stage with cirrhosis of the liver, jaundice, and ascites (Banti's disease)."

The case history of my patient, condensed from Dr. Slifer's ward notes, may be given briefly:

Summary. History of chills and fever in Italy two and a half years ago. Irregular fever, subsiding in hospital (acute bronchopneumonia); greatly enlarged spleen and liver; melanoderma; hæmic murmur; nasal, pulmonary, and gastrointestinal hemorrhages; marked anæmia with low hæmoglobin content; variable leukocyte count; malarial organisms found with difficulty and only after the administration of quinine.

Maria B., the patient herewith exhibited, is said to be fourteen years of age, but appears to be older. Although well developed and of Italian race, she has not yet menstruated. As she cannot speak English and an intelligent interpreter was lacking, little could be gleaned in the way of history or subjective symptoms when she was admitted to the Philadelphia General Hospital on December 12, 1903. She had at that time a slight fever, with pain in the chest and cough, accompanied with expectoration of blood-tinged mucus; and physical examination revealed signs—scattered areas of dulness, harsh breathing, subcrepitant rales, and friction sounds—that warranted a diagnosis of (influenzal?) bronchopneumonia, with concomitant pleurisy. The Widal reaction was not manifested in the blood or the diazo reaction in the urine, tubercle bacilli were absent from the sputum, which contained pneumococci, staphylococci, and streptococci. Enlargement of the spleen and enlargement of the liver were noted, as well as the presence of a faint systolic murmur at both base and apex of the heart. Malarial organisms were looked for and not found. The course toward recovery (of the acute attack) was uneventful. As cough, pain, and fever subsided, attention was given to the chronic conditions, and the outlines of spleen and liver carefully delimited by palpation and percussion. The lower border of the spleen was found to extend two inches to the right of the median line and three inches below the umbilicus. Thence the right border ran in a diagonal line toward the costal margin, which it cut one and a half inches to the right of the left mammillary line. Above the costal border percussion flatness extended to the fifth interspace in the mammillary line, to the sixth in the midaxillary line, and in the posterior axillary line to the lower border of the scapula in rest. The upper posterior corner of the splenic flatness was on the line of the upper border of the sixth dorsal vertebra, one inch to the left of the middle line of the back; thence the line extended diagonally forward to the posterior axillary line, which it cut at the margin of the ribs, there merging into the posterior border of the abdominal mass outlined by palpation.

The liver was found by percussion to reach to the eighth dorsal spine superiorly, inferiorly to the twelfth. Anteriorly the liver flatness in the mammillary line reached from the upper border of the fifth rib to a line one and a half inches below the costal margin. By palpation the liver was found to extend across the epigastrium as far as the right or anterior border of the spleen, when it apparently sank below the latter organ, which could be grasped separately. The abdomen as a whole was somewhat distended, the superficial veins well marked; there was no ascites; the conjunctivæ were slightly icteroid. The patient, as may be seen, is of dark skin, but has a deep red—not cyanotic—flush on both cheeks; the lips are of a good red color. Small pigmented areas are found over the entire body—the face, the neck, the thorax, the back, the arms, the abdomen, the legs, the soles of the feet. They vary in size from a pinhead to an irregular oval, whose long diameter may be one-half inch, and in hue from light yellow almost to black. The prevailing shade is a deep brown. On admission a history of constipation was given, but this symptom was absent while in the hospital; the bowel movements on admission being, indeed, liquid and of a light color.

January 3, 1904. The patient had a slight hemorrhage from the nose, which was followed by hæmoptysis, cough, and expectoration of blood, mostly bright red and frothy, though some clots were found. She did not complain of pain. Following the hemorrhage the pulse was rapid and rather weak and the area of splenic dulness seemed to be perhaps slightly decreased. Five days later the patient coughed up during the night about eight ounces of blood of a bright-red color, with a few small clots. In the morning epistaxis occurred, and the following night there was vomiting of about three ounces of partially clotted blood.

On January 10th the patient passed by bowel about six ounces of bloody fluid, described in the ward notes as "mostly pure blood, liquid and dark in color."

Examinations of the blood from the finger and of the urine were made from time to time, some of which may be quoted.

December 19, 1903. The urine was amber in color; acid in reaction; specific gravity 1016; sugar absent; trace of albumin present; no casts found.

January 21, 1904. The urine was reddish brown in color; acid in reaction; specific gravity 1014; sugar absent; albumen absent; no blood; no casts.

December 12, 1903. Hæmoglobin, 59 per cent.; red blood cells, 1,890,000; white blood cells, 23,450 (acute bronchopneumonia in active progress). Differential count of 200 leukocytes: small lymphocytes, 13.5 per cent.; large lymphocytes, 8.5 per cent.; polymorphonuclears, 77.5 per cent.; basophile, 0.5 per cent. An occasional megaloblast was observed; no malarial parasites demonstrable (Drs. Calhoun, J. C. Da Costa, Jr.).

January 1, 1904. Hæmoglobin 63 per cent.; red blood cells, 2,290,000; white blood cells, 14,000 (acute bronchopneumonia subsiding); no malarial parasites (Dr. J. C. Da Costa, Jr.). Widal's reaction, using dilution of 1 : 40, was negative in thirty minutes (Dr. Calhoun).

Failing to find malarial organisms it was decided, nevertheless, to begin treatment with the double hydrochlorate of quinine and urea, with the hope that this might perhaps disturb existing conditions in such a way that parasites might be found peripherally in accordance with an old clinical observation that in cases of latent malaria removal to a mountainous district or the administration and withdrawal of quinine would in many cases cause the development of frank paroxysms of ague.[1] Whether for this reason or for some other, Dr. Rosenberger's observation now detected the malarial organism.

14*th.* Hæmoglobin, 34 per cent. (following hemorrhage); red blood cells, 1,280,000; white blood cells, 10,400; nucleated reds present (Dr. Calhoun). Differential count of whites: polynuclear, 90 per cent.; lymphocytes, 6.5 per cent.; hyaline, 1.5; eosinophiles, 2 per cent.; microcytes, macrocytes, poikilocytes present; also a few macroblasts, normoblasts, and phantom reds; parasites present (Dr. Rosenberger).

22*d.* Hæmoglobin, 46 per cent.; red blood cells, 2,640,000; white blood cells, 7420 (after subsidence of acute bronchopneumonia); parasites present.

26*th.* Hæmoglobin, 48 per cent.; red blood cells, 2,690,000; white blood cells, 7800; nucleated reds present; parasites present (Dr. Calhoun).

The further description of the blood will be found in Dr. Rosenberger's report herewith appended.

Quinine having been withdrawn, treatment with arsenic was begun, Fowler's solution being pushed apparently to the point of tolerance as manifested by œdema of the eyelids and face. The dose, however, at which this symptom occurred was very small, about 10 minims three times daily. The arsenic was intermitted for a week, and then resumed, when after a few days of small doses the recurrence of œdema was noticed. Arsenic was then withdrawn entirely and remembering an old observation by J. M. Da Costa on the effect of ergot in diminishing malarial spleens, this drug was given in ascending doses, beginning with ten drops of the fluid extract and reaching thirty drops three times daily. Œdema, however, continued to recur and disappear during the administration of ergot, and it was then concluded that this was a phenomenon of the case itself, having no relation to the administration of drugs.

[1] I first read of this fact in Archibald Billings' First Principles of Medicine, London, 1838, p. 218; sixth edition, 1868, p. 433.

To test the point the ergot was suspended and arsenic again given, the œdema continuing to appear and disappear during the persistent administration of arsenic and during the withdrawal of arsenic. As the hemorrhages ceased and the patient began to gain in strength an *x*-ray picture was made. The patient was not at all incommoded by the examination, and the thought was suggested of attempting to use the therapeutic influence of the rays. She was accordingly treated twice weekly by Dr. Johnson with Roentgen radiations from a low-vacuum tube at a distance of twelve inches from the spleen; the period of exposure at first being five minutes, gradually increased to ten minutes. In addition, our object being not a therapeutic study, but an attempt to help the patient if possible, treatment with quinine and urea hydrochlorate was resumed, 15 grains being given by hypodermic injection daily, with instruction to cease when symptoms of cinchonism should be manifested. These have not appeared up to date, but the injections have nevertheless been discontinued on account of the local pain caused, and the drug is given by the mouth instead. In this connection W. J. Morton's observations on the therapeutic value of "internal fluorescence" through conjoint use with Roentgenism of quinine, fluorescin, æsculin, etc., are to be remembered.

Whether from rest, from nutrition, from *x*-rays, from ergot, from arsenic, from quinine, or from all these combined, or despite them, a great improvement has taken place in the condition of the patient. She is bright and cheerful; hemorrhages have not recurred since the date last noted, and the spleen and liver have diminished in size to the extent shown by the markings herewith exhibited, by which it will be seen, to be brief, that the outer border of the spleen has receded about two inches all around from the previous abdominal markings and that the liver extends but seven-eighths of an inch below the border of the ribs instead of one and a half inch as previously. Unfortunately our therapeutic observation cannot be continued, as the Immigration Commissioners claim the girl, as a public charge, for return to Italy.

The report of the blood examinations by Dr. Rosenberger, and his comments thereon, follow:

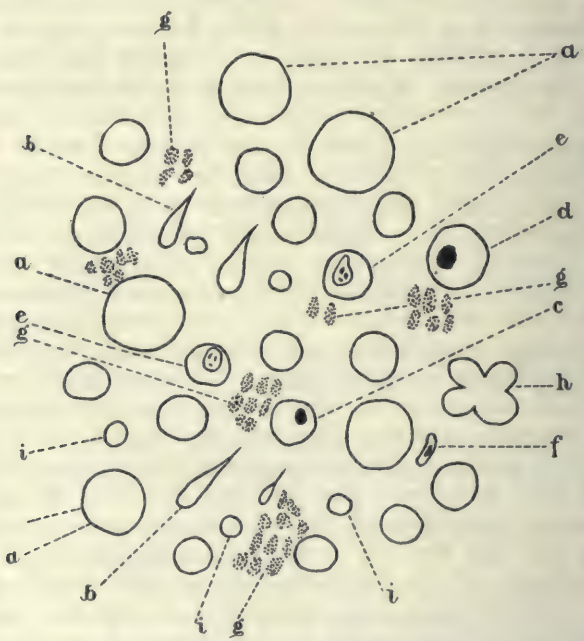
January 14th. The blood was thin, watery, pale, and of retarded coagulability. In the fresh state the erythrocytes were irregular in size and shape; microcytes, macrocytes, poikilocytes, nucleated forms (normoblasts and macroblasts) and a few pale or indistinct cells were present. There was no apparent increase of white cells, and the polymorphonuclear form was the most prominent.

In the preparation were a number of small bodies, some circular, some slightly oval. Some of these bodies were slightly granular, though most were hyaline. A few contained small fine pigment granules in an amotile state; some were intracellular, while the

greater number were extracellular. Hæmoglobin, 34 per cent. (Dare's hæmoglobinometer); erythrocytes, 1,280,000; leukocytes, 10,400 (Dr. Calhoun).

Spreads were stained with Ehrlich's triple mixture, some with Wright's, and others with Jenner's stain. A differential count of the leukocytes resulted as follows: polymorphonuclear, 90 per cent.; lymphocytes, 6.5 per cent.; hyaline cells, 1.5 per cent.; eosinophiles, 2 per cent.

In these stained preparations the bodies above referred to were plainly visible, mostly extracellular and possessing a finely granu-



a. Megalocytes. *b.* Poikilocytes. *c.* Normoblasts. *d.* Megaloblasts. *e.* Intracellular parasites. *f.* Extracellular parasite suggestively crescentic. *g.* Blood platelets. *h.* Deformed erythrocyte. *i.* Microcytes.

lar, faintly reticulated appearance. Ross' method was also used to demonstrate the parasites with success. Suggestively crescentic-shaped bodies were present.

20*th*. At this examination the blood presented the same interesting features.

In fresh preparations were the small hyaline bodies as noted in the first specimen, several of which were slightly motile.

There were few poikilocytes; an occasional nucleated red cell (normoblast) and a few phantom cells were still present, as well as the condition of microcytosis and macrocytosis. In spreads prepared with Wright's stain the bodies were evident; in some there was a

background or matrix staining an extremely delicate or pale blue. Hæmoglobin, 45 per cent. (Dare's hæmoglobinometer); erythrocytes, 2,640,000; leukocytes, 7420 (Dr. Calhoun). Differential count of leukocytes was: polymorphonuclear, 77.5 per cent.; lymphocytes, 14 per cent.; hyaline cells, 5.5 per cent.; eosinophiles, 2.5 per cent.; basophiles, 0.5 per cent.

In one or two hyaline cells an apparent nucleolus was situated eccentrically. Only two normoblasts were found in each of several spreads examined.

23*d*. Spreads of the blood were made at twelve o'clock (noon), 2 P.M., 4 P.M., and 6 P.M. In the fresh condition a few spherical hyaline, sluggish bodies were seen in each preparation. There seemed to be no increase in number in the succeeding examinations.

27*th*. The blood obtained upon this date differed in no respect from that taken four days previously. The bodies were clearly hyaline in the fresh blood, and in the stained spreads a few were seen intracellularly and faintly pigmented.

The irregularity in the size of the erythrocytes still persisted, while an occasional normoblast was seen. Apparent vacuolation of the red cells was also observed. Hæmoglobin, 47 per cent. (Dare's hæmoglobinometer); erythrocytes, 2,240,000; leukocytes, 6600. Differential count of the leukocytes was: polymorphonuclear, 66 per cent.; lymphocytes, 25.5 per cent.; hyaline cells, 6.5 per cent.; eosinophiles, 2 per cent. None of the leukocytes contained pigment granules.

30*th*. Spreads made upon this date contained the same bodies in about the same condition as in the previous examinations, mostly oval and extracellular, but a few were intracellular. Microcytes and macrocytes, phantom cells, apparently vacuolated erythrocytes, and an occasional normoblast were demonstrable. A few erythrocytes were seen taking the form of a four-leafed clover.

Some brief comment may be made upon the findings as thus detailed and as exhibited in the slides now under the microscopes.

Our blood picture may be summarized as follows: hæmoglobin, below 50 per cent.; erythrocytes, averaging 2,000,000; leukocytes, averaging between 7000 and 8000; poikilocytosis, microcytosis, and macrocytosis, presence of normoblasts, a few megaloblasts, phantom cells, and the appearance of small, oval, circular intracellular and extracellular bodies, which, in a small number, are very lightly pigmented.

In most respects the blood changes here recorded resemble those of Banti's disease or splenic anæmia, the chief differences being in the small number of nucleated reds found in this case and the absence of marked leukopenia. The low percentage of hæmoglobin, the small number of erythrocytes, the presence of poikilocytes, microcytes, macrocytes and phantom cells, all point to this

malady. Also the hæmatemesis and enterorrhagia are symptoms which clinically suggested Banti's disease. These latter conditions may have arisen from pressure bringing about congestion as a result of enlargement of the spleen. It is possible that we may be dealing with both maladies—*i. e.*, Banti's disease and malaria.

In morphology, the small bodies while not conforming to a typical malarial parasite, may represent, as Manson says, "moribund or fragmented forms." (These are mechanically freed parasites expressed from blood corpuscles by the compression to which the blood is subjected between slip and cover glasses. Frequently, these artificially freed parasites are broken into small fragments, and becoming free in the liquor sanguinis, assume a spherical or disk-like form. The protoplasm becoming diffluent, the pigment is resolved into a number of minute dust-like particles possessing active brownian movement.) The intracellular forms are no doubt malarial parasites.

Golgi describes as quinine forms of the malarial parasite certain rounded, immobile bodies with clumped pigment and sharp irregular outline, and deformed segmenting bodies deficient in the number of spores.

Ewing has observed in cinchonized cases half-grown forms numerously subdivided and deficient in chromatin.

That these bodies are piroplasma (Leishman-Donovan) seems doubtful, as the latter possess a micronucleus and macronucleus, are extremely small, are rarely, if ever, situated intracellularly (red cells), and are never found in the peripheral circulation.

According to most observers, the leukocytes in malaria do not increase in number, usually remaining below 10,000, and the polynuclear cells are most numerous in differential counts made.

Lymphocytosis may also occur in some cases. In pernicious malaria as low as 40 per cent. of polynuclear cells has been found by Bastianelli.

Various changes in the erythrocytes have been noticed by many observers. Oligocythæmia, erythropyknosis, granular degeneration, as well as phantom cells, macroblasts and microblasts have been observed. Ewing states that, as a rule, in cases of moderate severity there are changes in the red cells as noted in secondary anæmia. Hæmoglobin is also lowered in percentage.

In the case herein reported, there was never what might be called a marked leukocytosis, no lymphocytosis, nor was there ever evidence of pigment or the presence of any of the parasites in any of the leukocytes.

Throughout the differential counts made the polynuclear forms were most abundant. An occasional nucleolus eccentrically situated in one or two hyaline cells, and buds of protoplasm from lymphocytes were present. Occasionally a cell, reacting like a plasma cell, was found. The red cells in the first count were slightly less

than 2,000,000; in the second and third counts there were between 2,000,000 and 3,000,000. Large clusters of small, irregularly oval granular bodies, some reacting positively to the basic dye, others to the acid dye; some intracellular and others extracellular, represented in all probability degenerating blood platelets. They were in excessive numbers.

THE LEUKOCYTOSIS OF PREGNANCY, OF THE PUERPERIUM, AND OF ECLAMPSIA.

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Despite the numerous observations already published upon the leukocytosis of pregnancy and of the puerperium, it has seemed to us permissible to add our results to those of others, because of the very considerable variation in the reports of the different observers and because we wished to establish, for ourselves, a definite basis for the estimation of the leukocytosis of eclampsia.

1. The Leukocytosis of Pregnancy. The results given below are based upon 50 cases in the ninth month of pregnancy:

Average count	10,600
Highest count	18,400
Lowest count	5,400
Average in primiparæ	11,854
Average in multiparæ	9,346
Absence of leukocytosis	9

These counts were all taken on patients who were perfectly normal and were made from four to five hours after the mid-day meal, in order to eliminate, as far as possible, the question of digestive leukocytosis.

Digestive Leukocytosis in the Ninth Month of Pregnancy. It has been claimed by at least one observer, Rieder (Ewing), that in the ninth month of pregnancy there exists not only no digestive leukocytosis, but an actual decrease in the leukocytes.

In 20 cases studied by us the following results were obtained:

Digestive leukocytosis	in 13 cases.
No change	in 1 case.
An actual decrease	in 6 cases.

These counts were made one hour before and three hours after the mid-day meal.

2. The Leukocytosis of the Puerperium. The results given below are based upon 50 cases on the third day of the puerperium,

These cases all ran normal temperatures throughout, and at no time was there odor to the lochia:

Average count	12,400
Highest count	20,400
Lowest count	5,600
Average in primiparæ	13,200
Average in multiparæ	11,600
Absence of leukocytosis	8

The increase in the leukocytes during pregnancy and the early puerperium we believe to be largely due to the natural increase in the metabolic activity of the body at these periods.

3. The Leukocytosis in Eclampsia. These results tabulated below are based upon the leukocyte counts in 14 consecutive cases of eclampsia treated in this hospital, in the service of Dr. Edwin B. Cragin, during the past few months.

Inasmuch as so little work has as yet been published on this subject, we give the individual leukocyte counts of each of the 14 cases, with a brief synopsis of each case. The condition of the urine in the several cases has been purposely omitted as having no direct bearing upon the subject at hand.

We have divided these cases into three groups, according to the apparent degree of their toxicity.

Group A (mild). Case 1 (History No. 14110).—Patient developed eclampsia shortly after a normal labor. She had six convulsions the day after labor; her general condition, however, remaining good. Her recovery was uneventful from this time on.

Day of disease.	White blood-corpuscles.	Temperature.
1 post-partum	19,000	98° F.
2 "	18,200	100
3 "	16,000	98
10 "	13,200	100.4
14 "	9,400	99.6

Case 2. (History No. 14,164).—Patient also developed eclampsia a few hours after labor. On the day of delivery she had three severe convulsions. The next day the patient was quiet and conscious. Convalescence soon set in.

Day of disease.	White blood-corpuscles.	Temperature.
Delivery	21,600	98.4° F.
1 post-partum	15,200	99.2
2 "	13,400	99
5 "	8,400	99.2

Case 3 (History No. 14236).—The patient had four convulsions before admission. An *accouchement forcé* was performed. During the first day after delivery she had nine convulsions. Despite this large number of convulsions, her general condition remained fairly good. On the second day she became conscious and had no further convulsions. There was marked improvement on the third day, and uninterrupted convalescence thereafter.

Day of disease.	White blood-corpuscles.	Temperature.
Delivery	17,200	101° F.
1 post-partum	14,600	100.6
2 "	13,600	99.2
3 "	21,200	99.8
6 "	16,400	100
8 "	12,000	99.2
10 "	7,300	98.4

The temperature on the day of delivery was reactionary.

CASE 4 (History No. 14207).—The patient had several convulsions before admission. Her condition was very good for an eclamptic. She had a normal labor. There were no convulsions after delivery. Recovery was rapid.

Day of disease.	White blood-corpuscles.	Temperature.
Delivery	16,000	99.4° F.
1 post-partum	14,200	99.8
2 "	11,400	99
5 "	12,000	98.6
10 "	8,400	98.6

This was an especially mild case, and shows well the low leukocytosis in the mild type of the disease.

CASE 5 (History No. 14026).—The patient had six convulsions before admission. An *accouchement forcé* was performed. There were no convulsions after the delivery. Although in poor shape at first, she showed good resistance and convalesced rapidly.

Day of disease.	White blood-corpuscles.	Temperature.
Delivery	31,400	99.2° F.
1 post-partum	19,200	99
3 "	17,400	100.6
8 "	15,000	100
11 "	12,000	99.6
20 "	9,000	98.4

CASE 6 (History No. 14473).—The patient had four convulsions before admission. An *accouchement forcé* was performed. No convulsions after delivery. Patient had good resistance and convalesced satisfactorily.

Day of disease.	White blood-corpuscles.	Temperature.
Delivery	31,000	100.4° F.
1 post-partum	29,800	99.2
2 "	19,600	99.2
3 "	14,800	99.8
1 "	12,600	99
10 "	9,200	99

Group B (*severe*). CASE 7 (History No. 14147).—Patient had several convulsions before admission; condition very toxic; *accouchement forcé* was performed. She had two convulsions soon after delivery. Twenty-four hours after labor there was general improvement, and convalescence set in. There was, however, a setback on the fourth and fifth days, due, evidently, to increased hepatic irrita-

tion, as evidenced by severe pain in the region of the liver; nausea and slight vomiting of coffee-ground material.

Day of disease.	White blood-corpuscles.	Temperature.
Delivery	28,000	99.8° F.
1 post-partum	26,000	100
2 "	27,000	100.2
4 "	45,000	103
5 "	40,400	99
6 "	32,200	99.2
7 "	26,800	99
8 "	16,600	100
9 "	12,200	98.4
12 "	9,800	98.8

The temperature on the fourth day post-partum only lasted for four hours and was evidently due to a sudden, temporary increase in the toxic symptoms of the patient. The uterus was normal. The lochia normal in amount and without odor. The rise of the leukocytes on the fourth day was due to the aggravated condition of the patient.

Case 8 (History No. 14341).—The patient had several convulsions before admission; appeared very toxic. An *accouchement forcé* was performed. The following day there was considerable improvement; patient was rational at times. The second day there was marked pain in epigastric region, with some distention. The third day patient appeared worse; she vomited frequently small quantities of coffee-ground material. The fourth day the vomiting continued, but was less severe. The sixth day there was general improvement, with no further vomiting. From this time on there was steady improvement.

Day of disease.	White blood-corpuscles.	Temperature.
Delivery	36,000	101° F.
1 post-partum	26,600	98.6
2 "	33,200	100.6
3 "	32,000	100
4 "	23,400	99
6 "	23,600	99.4
8 "	19,000	100
10 "	14,000	99.4
14 "	9,200	99

The temperature of the day of delivery was a reactionary one. The rise of leukocytes on the second day after delivery was due to an aggravation of the symptoms.

Case 9 (History No. 14374).—The patient had five convulsions before admission. She was in labor and was delivered with forceps. There were nine convulsions on the first day after labor; but there were none after that. On the second day after labor, despite the fact that there were no convulsions, the patient's general appearance looked less favorable (this accounts for the rise in leukocytes). On the third day there was a turn for the better, and improvement continued uninterrupted.

Day of disease.	White blood-corpuscles.	Temperature.
Delivery	24,800	99.4° F.
1 post-partum	25,600	100.2
2 "	49,800	101
3 "	31,000	99.2
4 "	12,600	98.6
6 "	7,800	98.6

The rise of temperature on the second day was due again to the general toxic condition of the patient. There were positively no uterine symptoms.

Case 10 (History No. 14513).—There were four convulsions the day of admission. An *accouchement forcé* was performed. Patient looked very toxic, indeed; she continued in bad condition for the following two days, but then began to improve, and convalesced satisfactorily.

Day of disease.	White blood-corpuscles.	Temperature.
Delivery	46,000	99.6° F.
1 post-partum	37,600	99.2
2 "	30,000	99.6
3 "	27,200	98
6 "	16,000	98.4
8 "	13,800	98.8
14 "	7,400	98.8

This shows well strong resistance with a high leukocytosis in a severe case.

Case 11 (History No. 14183).—There were several convulsions before admission. Patient looked very badly. She was delivered with forceps. She had no convulsions after delivery, but all active treatment for two days had to be given with the patient under chloroform, as her condition was one of great irritability. Convalescence then set in and progressed satisfactorily.

Day of disease.	White blood-corpuscles.	Temperature.
Delivery	19,800	100.8° F.
1 post-partum	25,200	98
2 "	21,000	99.6
5 "	20,600	99.4
6 "	18,200	99.2
7 "	16,200	99.8
8 "	11,400	100
12 "	8,400	98

This case is given under "Group B," as the patient was, for at least thirty-six hours, in a critical condition, despite the relatively low leukocyte count.

Case 12 (History No. 14466).—The patient had a large number of convulsions before admission. Her condition appeared very grave. An *accouchement forcé* was performed. There were no convulsions after delivery, but for several days the prognosis was very uncertain. By the sixth day she began to improve rapidly, and was discharged in good condition, although her mind remained slightly clouded

Day of disease.	White blood-corpuscles.	Temperature.
Delivery	54,000	105° F.
1 post-partum	47,000	102
2 "	43,000	98
3 "	38,400	100.8
4 "	34,600	99.2
5 "	31,200	100
6 "	24,600	100.2
8 "	19,000	99.4

The temperature during the first two days was due to the intensity of the disease. The high leukocytosis illustrates well the strong resistance of the patient.

Group C (*very severe*). CASE 13 (History No. 13975).—The patient was admitted in very grave condition. She had several convulsions before entering the hospital and appeared hopeless from the start. An *accouchement forcé* was performed. She died two days after delivery from her toxæmia, having had no convulsions since delivery.

Day of disease.	White blood-corpuscles.	Temperature.
Delivery	19,600	100.2° F.
1 post-partum	15,400	99.8
2 "	13,800	99

We see here a case with extreme toxæmia and *poor* resistance and a *low* leukocyte count.

CASE 14 (History No. 14290).—Patient came into the hospital in labor. She developed eclampsia soon after delivery. The day of delivery she had twelve convulsions, and soon appeared deeply toxæmic. On the first day after labor there were no convulsions; the patient was conscious and appeared decidedly improved. On the second day after labor she became markedly worse; there was vomiting of blood and blood in the stools. Death took place on the evening of the second day.

Day of disease.	White blood-corpuscles.	Temperature.
Delivery	26,000	106° F.
1 post-partum	106,000	99.8
2 "	{45,200 / 35,800}	98.4

Here we have a patient with extreme toxæmia and with *good* resistance at first; this resistance, however, suddenly giving away, as is shown by the very rapid fall in the leukocytes.

CONCLUSIONS. While we appreciate the danger of drawing rash inferences from a rather limited number of cases, still, we deem it justifiable to formulate the following from the cases cited above:

1. The toxins of eclampsia cause, in most instances, a leukocytosis. The exact cause of this it is as yet impossible to explain.

2. All things being equal, the degree of the leukocytosis seems to depend very closely upon the degree of toxicity of the patient (*vide* Cases Nos. 3, 4, 10, and 12).

3. The greater resistance of the patient, the higher the leukocytosis (*vide* Cases Nos. 10 and 12).

4. A sudden increase in the leukocytes generally indicates an aggravation of the disease in an individual with good resistance (Cases Nos. 7, 9, and 14 show this especially well).

5. A low leukocyte count in a highly toxic patient is of bad omen (*vide* Case No. 13).

6. A leukocytosis originally high that falls rapidly in a badly toxic patient is likewise a danger signal (*vide* Case No. 14).

7. There is no direct relation between the leukocyte curve and the temperature curve.

REMARKS. 1. These observations were all made with especial care, so as to eliminate any errors of technique. In cases with an unusually high count the determination was verified by a second man.

2. These cases were all devoid of the least evidence of uterine infection.

THE RELATION OF THE ISLANDS OF LANGERHANS TO DISEASES OF THE LIVER, WITH SPECIAL REFERENCE TO CARBOHYDRATE METABOLISM.

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WARTHIN,[1] reporting a case of primary adenocarcinoma of the gall-bladder in which there was marked involvement of the liver by tumor secondaries, directs particular attention to the enlargement of the pancreas in the case. In view of the fact that there was but little evidence of inflammation to be found in the pancreas, he concluded that he was dealing with a true hypertrophy of that organ. Not only does he believe the condition to have been a true hypertrophy, but one compensatory in nature, amending the lost or limited liver function. The islands of Langerhans in this pancreas were from three to five times their usual size.

A case quite similar in anatomical features came to my notice in November, 1901. In it the histological features of the pancreas are almost identical with those in Warthin's case. (See Case I.) At that time my chief interests lay in the consideration of the enlargement of the islands of Langerhans. These structures were carefully measured in sections from various parts of the pancreas. The conclusions then reached concerning the true significance of the hypertrophy of these islands are herewith appended. (See Conclusions 1 and 2.) Nothing further was done with this material until recently,

[1] Philadelphia Medical Journal, July 7-14-21, 1900.

when my interest was reawakened by finding, in one of our Independence Hospital cases, an immense increase in size of the Langerhans' islands, the enlargement being apparently coincident with or subsequent to a marked destruction of the liver parenchyma. (See Case II.)

The study of sections from the liver and pancreas from a number of cases which we have had here since July 1, 1902, also a considerable number of sections of liver and pancreas furnished me by Dr. Ludwig Hektoen from cases in which the liver showed more or less marked involvement by various disease processes, was now undertaken. An attempt will here be made to briefly describe the histological features of the liver and pancreas from such cases as most clearly illustrate the point I wish to make concerning the true significance of the enlargement of the islands of Langerhans. Only the more important anatomical findings will be given, together with a brief description of the gross appearance of the liver and pancreas, in a few cases. The Zeiss micrometer eye-piece was used in making the measurements of the islands of Langerhans. At least five islands of varying sizes were measured in each section and the average then obtained. In none of the following cases was sugar found in the urine:

Case I.—Mrs. L. T., aged thirty-eight years. Admitted to the service of Dr. T. J. Watkins, Mercy Hospital, Chicago, October 4, 1901; died October 9, 1901. The immediate autopsy was performed by Dr. George de Tarnowsky, and the material was sent to the Department of Pathology, Northwestern University Medical School, where I examined it under the direction of Dr. A. P. Ohlmacher.

Anatomical Diagnosis. Primary adenocarcinoma of gall-bladder, with metastases of liver, lungs, and abdominal, cervical, axillary, and inguinal lymph glands; cholelithiasis; fatty myocarditis; chronic parenchymatous nephritis; ascites.

Liver. The liver weighs nineteen pounds. The surface is studded with yellowish nodules, varying in cross-section from the size of a split pea to a half-dollar piece. Some of the nodules present smooth surfaces and are firm; others are softened and umbilicated. The liver cuts with increased resistance. The incised surface is studded with large and small, discrete and conglomerate tumor nodules. There are many areas of hemorrhagic softening. The bile channels are dilated and apparently filled with bile, giving the liver substance a greenish-yellow hue. The common duct is patent.

Histology of Liver. Epithelial cells in gland-like arrangement, separated by dense bands of fibrous tissue varying in width, are found throughout the liver. Areas of necrosis are frequent; hemorrhagic foci are also of frequent occurrence and widely separated areas of liver cells are found. These cells show more or less degeneration; some of them contain much fat and practically all contain bile pigment. The bile channels are dilated and filled with bile.

Pancreas. The pancreas is large and firm. It cuts with somewhat increased resistance. The cut surface, however, shows no increase of fibrous tissue. The pancreatic duct is patent.

Histology of Pancreas. The interlobular and interacinous tissue is normal in amount. The acini are abundant and are closely packed together. The cells composing them show no degeneration. The islands of Langerhans are everywhere greatly enlarged and well defined. Those in the tail of the pancreas are more abundant and somewhat larger than the ones found elsewhere. The cells composing them are slightly more granular than usual. The measurements of the islands are as follows: largest, 0.4 mm.; smallest, 0.07 mm.; average, 0.255 mm.

CASE II.—Otto J., aged sixty-three years. Admitted to the Independence State Hospital, January 6, 1881; died April 19, 1903.

Anatomical Diagnosis. Chronic valvular endocarditis; double hydrothorax; ancient pleuritis; diffuse carcinomatous infiltration of pylorus, with metastases of liver, lungs, head of pancreas, and abdominal lymph glands; cholelithiasis; obliteration of common bile duct; chronic, diffuse nephritis.

Liver. The liver weighs 2370 grams. It is much firmer than ordinary. A few large and small tumor nodules are scattered over the liver surface, some of them being umbilicated. Hemorrhagic foci, varying greatly in size, are also abundant. The liver cuts with increased resistance. The cut surface shows a few illy-defined tumor nodules, mostly large, a marked increase of fibrous tissue and many hemorrhagic foci. But few lobular markings are to be found. The common duct is obliterated.

Histology of Liver. From various parts of the liver, sections show a very marked increase of fibrous tissue, which has a loose reticulated appearance, or occurs in dense bands. Scattered here and there are epithelial cells in tube-like arrangement. No liver cells were found in any of the sections examined.

Pancreas. The pancreas is somewhat enlarged and quite firm. It cuts with increased resistance. Lying within the interlobular tissue, at the head of the pancreas, small, yellowish foci are seen, averaging about 1 mm. in diameter. The interlobular tissue appears to be slightly increased. Minute, rounded, well-defined foci are seen within the lobules. (These small foci within the lobules, on microscopic examination, are seen to be greatly enlarged islands of Langerhans.) The pancreatic duct is patent.

Histology of Pancreas. In the head of the pancreas considerable increase of interlobular fibrous tissue exists in places, thus destroying many of the acini. In other areas the interlobular tissue is normal in amount. The interacinous tissue is slightly increased. Masses of epithelial cells, resembling those found in the tumor of the pylorus, appear in the interlobular lymph channels. None of these cells invade the lobules. In some places the cells of the acini

show considerable fatty degeneration. The islands of Langerhans are immensely enlarged. Some of them are surrounded with quite dense fibrous tissue capsules. The cells composing these islands are more granular than usual. There is a slight proliferation of fibrous tissue within the interacinous cell groups. Sections taken from the body of the pancreas show a slight increase of interlobular tissue everywhere. The interacinous tissue appears normal. No tumor cells are found in sections from this area. Here, as in the head of the pancreas, the islands of Langerhans are greatly enlarged. Sections made from the tail of the pancreas exhibit the interstitial tissue normal in amount. In this region the islands of Langerhans are uniformly larger and more abundant than elsewhere. No areas of fat necrosis are found. The measurements of the islands of Langerhans are as follows: largest, 0.655 mm.; smallest, 0.095 mm.; average, 0.351 mm.

Case III.—William R., aged about fifty years. Admitted to the service of Dr. Fenger, Presbyterian Hospital, Chicago. Post-mortem by Dr. Crowder.

Anatomical Diagnosis. Primary carcinoma of gall-bladder; secondary carcinoma of liver and retroperitoneal lymph glands; cholelithiasis; obliteration of common bile duct.

Liver. "The liver is enlarged and firm. Scattered over the surface are large and small tumor nodules. The cut surface everywhere shows many large and small tumor nodules. The interstitial tissue is seen to be greatly increased. Bile pigment is abundant."

Histology of Liver. Sections from various parts of the liver show well-defined rounded areas of epithelial cells in gland-like arrangement. About these areas fibrous tissue is abundant. The interlobular tissue is universally increased. The remaining columns of liver cells are compressed, appear granular, contain bile pigment, and occasionally considerable fat. The central veins and tributaries are dilated and congested.

Pancreas. The pancreas is quite large and firm. It cuts with increased resistance. The pancreatic duct is patent.

Histology of Pancreas. In some areas the interlobular tissue is greatly increased, forming wide compact bands. The interacinous tissue is also increased, though to a degree less than the interlobular tissue. Where the fibrous tissue is most abundant no acini are found, but an island of Langerhans, or frequently several Langerhans' islands closely packed together, still remain. These islands are surrounded by dense fibrous bands. The most of the islands throughout the pancreas are very large. In some there is a very slight increase of fibrous tissue. Except for this, and the fact that the cells composing them are more granular, they appear normal. In certain areas from various sections of the pancreas the interlobular tissue is not so markedly increased. The acini in such areas appear normal, and the fibrous tissue around and within the islands

of Langerhans is not increased. The measurements of the islands of Langerhans are as follows: largest, 0.57 mm.; smallest, 0.171 mm.; average, 0.335 mm.

CASE IV.—William P., aged forty-nine years. Admitted to the service of Dr. James B. Herrick, Cook County Hospital, Chicago. Post-mortem by Dr. Hektoen.

Anatomical Diagnosis. Acute, general tuberculosis of lungs, kidneys and retroperitoneal lymph glands; right fibrinous pleuritis; nodular sclerosis of aorta; cirrhosis of liver; cholelithiasis; ascites.

Histology of Liver. The interlobular and intralobular tissue is much increased. Within this tissue lymphoid cells are abundant. The intercellular capillaries are dilated. Some of the liver cells in the lobules have entirely disappeared. The cords of liver cells remaining are atrophic, widely separated, and show a granular degeneration.

Histology of Pancreas. The interlobular and interacinous tissue is only slightly if at all increased. A few lymphoid cells are present in the interacinous tissue. Many of the groups of acini seem to be undergoing a transition into islands of Langerhans, such as has been described by Lewaschew and others.[1] Areas of post-mortem digestion are seen. The islands of Langerhans are very prominent and abundant. The cells composing them are large, closely packed and granular. The capillaries within these islands are slightly dilated. The measurements of the islands of Langerhans are as follows: largest, 0.341 mm.; smallest, 0.114 mm.; average, 0.237 mm.

CASE V.—Kannute E., aged seventy years. Admitted to service of Dr. Danielson, Norwegian Hospital, Chicago. Post-mortem by Dr. H. G. Wells.

Anatomical Diagnosis. Advanced, atrophic cirrhosis of liver; primary carcinoma and multiple adenoma of liver; chronic interstitial nephritis; fibrous myocarditis; general arteriosclerosis; pericholecystitis; perityphlitis; cholelithiasis.

Histology of Liver. There is a marked increase of interlobular tissue, which contains many lymphoid cells. Numerous small well-defined areas of cells in gland-like arrangement are found in various sections of the liver. Within and about such areas the liver cells are destroyed. The remaining liver cells are granular, and a few show fatty degeneration. The bile ducts appear to be increased in number. The areas of cells found in this liver which show the gland-like arrangement have been described by H. G. Wells,[2] in this case, as primary carcinoma, and in some of them it is possible to make out a transition of the liver cells into the adenomatous tumor structure Wells describes.

Histology of Pancreas. The interlobular tissue appears about normal in amount. The interacinous tissue shows a very slight and

[1] Opie. Diseases of the Pancreas, pp. 81–85.

[2] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, No. 3, vol. cxxvi. pp. 403–417.

uniform increase; it contains some lymphoid cells. The islands of Langerhans are prominent, and are closely packed with their characteristic cells. The lumina of many of the acini are filled with homogeneous material staining light red with eosin. The measurements of the islands of Langerhans are as follows: largest, 0.361 mm.; smallest, 0.228 mm.; average, 0.324 mm.

Case VI.—William Z., aged fifty-three years. Admitted to the service of Dr. Billings, Presbyterian Hospital, Chicago. Post-mortem by Dr. Crowder.

Anatomical Diagnosis. Chronic interstitial nephritis; hypertrophic cirrhosis of liver and spleen; chronic localized peritonitis and perisplenitis; hydrothorax; hydropericardium; ascites.

Histology of Liver. The interlobular tissue is markedly increased; lymphoid cells are abundant. The liver cells are atrophic, granular, and occur in small, isolated masses.

Histology of Pancreas. The interlobular and interacinous tissue is normal in amount. The islands of Langerhans are large, but not very abundant. The cells composing them are granular and closely packed. Areas of post-mortem digestion are seen in various parts of the sections examined. The measurements of the islands of Langerhans are as follows: largest, 0.304 mm.; smallest, 0.095 mm. average, 0.209 mm.

Case VII.—Mary T., aged seventy years. Admitted to the Independence State Hospital August 9, 1902; died November 14, 1902.

Anatomical Diagnosis. Chronic endocarditis; fatty myocarditis; localized, double, old pleuritis; congestion of lungs; fatty degeneration of liver, with slight cirrhosis; pericholecystitis; obliteration of common bile duct; chronic diffuse nephritis; scirrhous carcinoma of left breast, with extension into left axillary glands.

Histology of Liver. The interlobular tissue is considerably increased. The central veins and tributary capillaries are much engorged with blood and dilated. The liver cells are shrunken, granular, and those near the periphery of the lobules are fatty.

Histology of Pancreas. The interlobular tissue is slightly increased. In some areas the interacinous tissue is slightly increased. There is much fat between the lobules. Here and there numerous lymphoid cells are found in the interlobular tissue. The acini are normal in appearance. Most of the islands of Langerhans are immensely enlarged. The cells composing them are granular. There is no proliferation of fibrous tissue within them. About some of these structures the fibrous tissue is considerably increased. The measurements of the islands of Langerhans are as follows: largest, 0.608 mm.; smallest, 0.19 mm.; average, 0.399 mm. The enlargement of the islands of Langerhans in this pancreas seems greater than the involvement of the liver would warrant.

Case VIII.—Norman M., aged ninety years. Admitted to the Independence State Hospital August 27, 1896; died October 21, 1902.

Anatomical Diagnosis. Fibrous myocarditis, with dilatation of right ventricle and auricle; sclerosis of coronary arteries; chronic, valvular endocarditis, with insufficiency of aortic valve; localized, double, old pleuritis; arteriosclerotic atrophy of kidneys; cyanotic induration and senile atrophy of spleen; general arteriosclerosis.

Histology of Liver. The interlobular tissue is slightly increased. In some areas the intralobular tissue is increased. Many of the liver cells show slight fatty changes and cloudy swelling. Bile pigment is present in considerable amount. The hepatic cells surrounding some of the bile channels are necrotic.

Histology of Pancreas. There is a slight but uniform increase of interlobular and interacinous tissue. A few lymphoid cells are found in this tissue. The bloodvessel walls are considerably thickened. Interlobular fat is increased in amount. The islands of Langerhans are large and some of them are surrounded by slightly thickened bands of fibrous tissue. The cells of the islands are more granular than normal, but otherwise appear unaltered. The measurements of the islands of Langerhans are as follows: Largest, 0.323 mm.; smallest, 0.133 mm.; average, 0.247 mm.

Case IX.—Elizabeth K., aged seventy-two years. Admitted to the Independence State Hospital April 5, 1902; died July 26, 1902.

Anatomical Diagnosis. Fibrous myocarditis; old pleuritis; general arteriosclerosis; papillomatous cystoma of right ovary, with abdominal metastases; ascites; induration, fatty degeneration and senile atrophy of liver; arteriosclerotic atrophy of kidneys; chronic pachymeningitis and leptomeningitis.

Histology of Liver. There is a slight increase of interlobular and intralobular tissue. The central veins and tributaries are dilated. The cords of liver cells are atrophic and granular. Many hepatic cells show fatty degeneration. Those about the central veins are quite generally destroyed.

Histology of Pancreas. In some places the interlobular tissue is slightly increased. In all but one area the interacinous tissue is of normal amount. One lobule is almost entirely replaced by newly formed fibrous tissue containing many lymphoid cells. Within this lobule are several islands of Langerhans, in which the connective tissue is slightly increased. Most of the islands of Langerhans throughout the pancreas are very large, and the cells composing them are granular. Otherwise they appear unaltered. Some of the cells of the acini show fatty degeneration. The measurements of the islands of Langerhans are as follows: largest, 0.38 mm.; smallest, 0.095 mm.; average, 0.25 mm.

Case X.—Phœbe P., aged sixty-four years. Admitted to the Independence State Hospital May 23, 1898; died August 8, 1902.

Anatomical Diagnosis. Hypertrophy of left ventricle of heart; chronic mitral and aortic endocarditis; old right-sided pleuritis; fatty degeneration of liver; diffuse meningeal hemorrhage.

Histology of Liver. The liver cells everywhere show a marked degree of fatty degeneration, many of them being greatly vacuolated. Bile pigment is of frequent occurrence within the cells. Areas in which the liver cells have entirely disappeared are scattered throughout various sections examined.

Histology of Pancreas. The interlobular and interacinous fibrous tissue appears normal in amount. The islands of Langerhans are numerous, enlarged, and the cells composing them are granular. Here and there are large and small areas of acini apparently undergoing a transformation into interacinous cell groups. The capillary bloodvessels are everywhere engorged with blood and can be traced about the acini and into the islands of Langerhans. The arrangement of the capillary bloodvessels about the columns of cells in the islands of Langerhans is identical with that about the acini. The measurements of the islands of Langerhans are as follows: largest, 0.323 mm.; smallest, 0.114 mm.; average, 0.218 mm.

Case XI.—Helen E., aged forty-one years. Admitted to the Independence State Hospital June 20, 1902; died August 7, 1902.

Anatomical Diagnosis. General anæmia; fatty degeneration of liver; punctate hemorrhage of liver (a case of pernicious anæmia).

Histology of Liver. The central veins and tributaries are dilated. The cords of liver cells are quite generally atrophic and in some places have entirely disappeared. Many of the remaining liver cells are somewhat fatty and contain bile. All of them are more or less granular. Many leukocytes are found in the capillary bloodvessels. A few small areas of hemorrhagic necrosis are found.

Histology of Pancreas. The interstitial tissue is normal in amount. The islands of Langerhans are much enlarged. The cells composing them are somewhat granular and are closely packed. The measurements of the islands of Langerhans are as follows: largest, 0.399 mm.; smallest, 0.114 mm.; average, 0.264 mm.

Case XII.—Mark C., aged twenty-eight years. Admitted to the Independence State Hospital August 30, 1902; died October 29, 1903.

Anatomical Diagnosis. Acute miliary tuberculosis of lungs, liver, spleen, and kidneys.

Histology of Liver. The liver cells show much fatty degeneration. Areas of necrosis are of frequent occurrence. Typical histological tubercles are also found. The interlobular and intralobular bloodvessels are engorged with blood.

Histology of Pancreas. The fibrous tissue is normal in amount. The islands of Langerhans are abundant, mostly large, and are closely packed with their characteristic cells. The measurements of the islands of Langerhans are as follows: largest, 0.368 mm.; smallest, 0.134 mm.; average, 0.227 mm.

Case XIII.—Helen K., aged forty-five years. Admitted to the Independence State Hospital April 8, 1902; died February 11, 1903.

Anatomical Diagnosis. Atrophy and fatty degeneration of heart; tuberculous bronchopneumonia; tuberculosis of peribronchial and mediastinal glands; old, right-sided, obliterating pleuritis; old, left-sided, localized pleuritis; amyloid infiltration of spleen; fatty degeneration of liver; chronic diffuse nephritis; tuberculous ulceration of small intestine, cæcum, and ascending colon.

Histology of Liver. The central veins and tributaries are much dilated and engorged with blood. There is marked fatty degeneration of the liver cells, especially at the periphery of the lobules. A pink-staining, homogeneous material is seen to occupy many of the cells throughout the various sections examined.

Histology of Pancreas. The fibrous tissue is normal in amount. The islands of Langerhans are very abundant and large. The cells composing them are granular. The capillary bloodvessels of these islands are slightly congested. The measurements of the islands of Langerhans are as follows: largest, 0.475 mm.; smallest, 0.095 mm.; average, 0.26 mm.

Case XIV.—Amelia L., aged thirty-six years. Admitted to the Independence State Hospital March 3, 1899; died November 9, 1902.

Anatomical Diagnosis. Old pleuritis; parenchymatous degeneration of heart muscle; chronic pulmonary tuberculosis; amyloid infiltration of spleen, liver, and kidneys; parenchymatous degeneration of pancreas; tuberculous ulceration of ileum and colon; tuberculosis of mesenteric glands.

Histology of Liver. Almost all the liver cells seen in the various sections contain a homogeneous material, staining pink with eosin, blue with Mallory's aniline-blue stain, and mahogany-red with Lugol's solution. But little evidence of fatty degeneration is seen.

Histology of Pancreas. The fibrous tissue is normal in amount. The cells of the acini show slight degree of fatty degeneration. The islands of Langerhans are large, numerous, well defined, and closely packed with their characteristic cells, which are more granular than usual. The bloodvessels of the pancreas are slightly congested. The measurements of the islands of Langerhans are as follows: largest, 0.465 mm.; smallest, 0.095 mm.; average, 0.29 mm.

Case XV.—Christian K., middle aged. Admitted to the Independence State Hospital February 7, 1899; died August 14, 1902.

Anatomical Diagnosis. Diffuse purulent peritonitis; tuberculous perforation of ileum; double pulmonary tuberculosis; amyloid infiltration of liver and spleen.

Histology of Liver. The liver cells have largely given place to a homogeneous material, staining pink with eosin and answering to the various tests for amyloid. The interlobular tissue is somewhat increased.

Histology of Pancreas. The fibrous tissue is normal in amount. A few lymphoid cells are found within this tissue. The cells of the

acini show some cloudy swelling and slight fatty degeneration. The islands of Langerhans are abundant, large and well defined. The cells composing them are granular and closely packed. The measurements of the islands of Langerhans are as follows: largest, 0.38 mm.; smallest, 0.114 mm.; average, 0.241 mm.

Besides the cases of which a brief description has been offered, 25 additional ones are herewith tabulated. An endeavor has been made to classify these cases according to the degree of involvement of the liver by disease processes, separating those in which there is an increase of fibrous tissue in the pancreas from such as present a normal amount of interstitial structure.

TABLE ILLUSTRATING ENLARGEMENT OF THE ISLANDS OF LANGERHANS FOLLOWING DISEASES OF THE LIVER. SUPPLEMENTAL TO CASES ALREADY GIVEN.

Marked chronic passive congestion of liver. Pancreas normal.

Age.	Largest island.	Smallest island.	Average size of islands.	Remarks.
48	0.304 mm.	0.100 mm.	0.2118 mm.	Very abundant.
39	0.342 "	0.067 "	0.207 "	Fairly "
39	0.380 "	0.190 "	0.2327 "	Very "
75	0.368 "	0.080 "	0.2034 "	" "
60	0.368 "	0.100 "	0.2208 "	" "
Average total . .	0.352+mm.	0.107+mm.	0.215 + mm.	

Marked chronic passive congestion of liver. Increase of fibrous tissue in pancreas.

Age.	Largest island.	Smallest island.	Average size of islands.	Remarks.
74	0.323 mm.	0.114 mm.	0.2217 mm.	Abundant.
40	0.323 "	0.100 "	0 2095 "	Fairly abundant.
67	0.335 "	0·08 "	0.1994 "	Abundant.
Average total . .	0.327 mm.	0,098 mm.	0.21 + mm.	

Slight chronic passive congestion of liver. Pancreas normal.

Age.	Largest island.	Smallest island.	Average size of islands.	Remarks.
80	0.268 mm.	0 134 mm.	0.201 mm.	Scarce.
61	0.301 "	0.100 "	0.2018 "	Fairly abundant.
54	0.285 "	0.133 "	0.109 "	" "
Average total . .	0.284 mm.	0.122 mm.	0 17 mm.	

Slight chronic passive congestion of liver. Increase of fibrous tissue within pancreas.

Age.	Largest island.	Smallest island.	Average size of islands.	Remarks.
63	0.285 mm.	0.095 mm.	0.209 mm.	Fairly abundant.
83	0.285 "	0.095 "	0 219 "	Very "
48	0.304 "	0 095 "	0.204 "	Fairly "
71	0.234 "	0.100 "	0.178 "	Scarce.
Average total . .	0.277 mm.	0.096+mm.	0.202 + mm.	

Focal necrosis of liver in case of streptococcus septicœmia. Acute interstitial pancreatitis.

Age.	Largest island.	Smallest island.	Average size of islands.	Remarks.
71	0.285 mm.	0.095 mm.	0.171 mm.	Abundant.

Considerable fatty degeneration of liver. Pancreas normal.

Age.	Largest island.	Smallest island.	Average size of islands.	Remarks.
43	0.285 mm.	0.095 mm.	0.182 mm.	Abundant. (See text.)

Slight passive congestion and acute parenchymatous degeneration of liver. Slight acute interstitial pancreatitis. (Case of urœmia.)

Age.	Largest island.	Smallest island.	Average size of islands.	Remarks.
26	0.456 mm.	0.19 mm.	0.327 mm.	Abundant. (See text.)

Liver practically normal. Pancreas normal.

Age.	Largest island.	Smallest island.	Average size of islands.	Remarks.
54	0.214 mm.	0.08 mm.	0.1623 mm.	Scarce.
42	0.268 "	0.067 "	0.1925 "	Fairly abundant.
26[1].	0.234 "	0.067 "	0.1088 "	Scarce.
53	0.228 "	0.095 "	0.1596 "	"
Average total . .	0.236 mm.	0.077 mm.	0.155 + mm.	

[1] This case is the only one of this particular series in which the liver shows no chronic changes.

Liver practically normal. Slight increase of fibrous tissue within pancreas.

Age.	Largest island.	Smallest island.	Average size of islands.	Remarks.
63	0.201 mm.	0.05 mm.	0.131 + mm.	Fairly abundant.
74	0.234 "	0.08 "	0.16 + "	" "
25[1].	0.201 "	0.10 "	0.117 + "	Scarce.
Average total . .	0.212 mm.	0.076+mm.	0.136 mm.	

By referring to the above table, it will be noticed that 8 cases are given in which the liver shows the changes of marked, chronic passive congestion. In 5 of these the fibrous tissue of the pancreas was normal in amount, while in 3 it was slightly increased. It will also be noticed that in those cases in which the fibrous tissue was normal in amount the islands of Langerhans, except in 1 case, were somewhat larger than those found in the 3 cases in which the fibrous tissue was increased. Thus, it will be apparent that chronic inflammatory changes could have had but little or no influence in the causation of the enlargement of these interacinous cell groups. This also holds true in a considerable number of other cases, as, for instance, Cases I., V., VI., IX., X., XI., XIII., and XV.

In 1 case (see table) the liver showed considerable fatty degeneration, and the islands of Langerhans did not appear to have enlarged to any considerable degree, though they were more abundant than usual. In this case we would expect, in view of the findings in the various cases above cited, that such a degree of liver involvement would be accompanied by enlargement of the interacinous cell groups of the pancreas. Possibly the fatty changes found in the liver of this case were of an acute type, and the islands of Langerhans had as yet failed to respond to the additional work thrown upon them because of the diseased condition of the liver. In another case (see table) the liver showed but a slight passive congestion and acute parenchymatous degeneration. There was a beginning acute interstitial pancreatitis. In this case the islands of Langerhans were greatly enlarged and numerous. Here the involvement of the liver is so slight that it cannot be held responsible for the great enlargement shown by the islands of Langerhans. The cause of death in this case was acute uræmia, the patient being a woman aged twenty-six years. Perhaps this condition may be held accountable for the phenomenon presented by the islands of Langerhans. While these 2 cases offer an exception to the rule established by our other examples, their number alone would seem insufficient to offer any valuable proof contrary to the point I wish to make regarding the relation of the islands of Langerhans to the diseases of the liver.

[1] This case is the only one of this particular series in which the liver shows no chronic changes.

That the relation between a diseased liver and hypertrophy of the islands of Langerhans is a close one is shown by the fact that in practically all of our cases the hypertrophy of these islands is proportionate to the degree of liver disease. The great abundance of the islands of Langerhans in many of these cases seems of importance as suggesting the ability of these structures to multiply. In fact, in some cases a transformation of the acinous glands into interacinous cell groups is apparently taking place. Opie does not believe it possible for the acinous cell groups to become converted into islands of Langerhans, as he was unable to prove, by animal experiments, that such a phenomenon really occurs. He also believes that the apparent increase in number of the islands of Langerhans seen in various cases is only a relative one due to the presence of unusual amounts of fibrous tissue, which, causing the atrophy of the individual lobules, brings the islands closer together, thus giving them the appearance of having multiplied. While this is probably true in many cases, it is not so in all, for occasionally I have found a pancreas with a normal amount of fibrous tissue in which the islands of Langerhans were very abundant.

Cases II., III., and VI., in which abundant fibrous tissue is seen around greatly enlarged, though otherwise unaltered, interacinous cell groups, not only illustrates Opie's observations as to the wonderful resistance these islands show toward inflammatory processes, but suggests the probability of these islands having enlarged before any marked increase of fibrous tissue had taken place about them. It would appear to be a mechanical impossibility for these structures, made up as they are by epithelial cells supported by a delicate framework of capillaries, to enlarge if hampered on all sides by fibrous tissue bands of increased thickness and density. Assuming that the enlargement of the islands of Langerhans is subsequent to the impairment of the liver function, we are safe in the deduction that the hepatic disease occurred some time before the involvement of the pancreas in the cirrhotic process, or, at the most, before the cirrhotic process in this viscus had become at all marked.

In almost all of the cases the cells of the islands of Langerhans are very abundant and somewhat more granular than usual. I am inclined to interpret this as due to an increased activity on the part of these structures, especially as Ssobolew has shown, after feeding dogs on carbohydrates, that the cells of the islands of Langerhans become granular, probably due to the increased demand placed upon them. In 7 cases (see table) the liver is stated as being practically normal. In all but 2 of these cases, however, some slight chronic changes are found. In these two exceptions the livers present only a slight degree of cloudy swelling.

I have, of course, not lost sight of the necessity of studying normal liver and pancreas to obtain a basis for comparison, so far as the material available to my purpose permits. The only reference to

the size of the normal islands of Langerhans that has been found is in Kölliker's *Handbuch der Gewebelehre des Menschen.*[1] Here the normal diameters of these structures are given as varying from 0.07 mm. to 0.3 mm. Unfortunately, no *average* measurement is given. The statement is made that the islands of Langerhans vary much in size and numbers; in some cases being small and scarce, in others being large and abundant. It seems probable, in those cases in which the islands of Langerhans are large and numerous, Kölliker was dealing with abnormal conditions. It appears wholly improbable that such a degree of enlargement as 0.3 mm. is ever attained by these structures except under abnormal conditions, such, for example, as that described in this text.

We may now enter upon the consideration of the significance of the enlargement of the islands of Langerhans in the above-cited cases. That this enlargement is a true hypertrophy, and, further, an hypertrophy compensating for some lost or limited liver function, subsequent to disease processes in that viscus, is highly probable. Opie's observations have shown that, in so far as the pancreas is concerned, the carbohydrate function is controlled by the islands of Langerhans. Furthermore, this seems to be their *sole* function. This being the case, a compensatory hypertrophy on their part can only be brought about by an impairment of a similar or complimental function on the part of some other organ or organs. Since the discovery of Claude Bernard in 1853, that the liver normally contains as much as 40 per cent. of glycogen, abundant clinical and experimental evidence has demonstrated the very important carbohydrate function possessed by this organ. The function of the liver, of converting the carbohydrates of ingestion and the sugars of digestion into glycogen and there to retain this product for the body's future use, together with its property of reconverting this glycogen into sugar (dextrose and levulose), supplying it to the blood according to the tissues' needs, is fully established. The sugar content of the blood (about 0.02 per cent.) is thus regulated. With the above facts in view, many observers believe (though less than formerly) that with a perverted glycogenic function of the liver, glycosuria, and not infrequently diabetes, results.

"Two theories concerning the role the liver plays in the causation of glycosuria have arisen. One theory supposes a depressed glycogenic function in the liver: that the liver cells are unable to convert the digestive sugars (dextrose and levulose) brought to them by the portal blood into glycogen, and that in consequence sugar accumulates in the blood (hyperglycæmia) in greater quantities than can be made use of by the tissues, to be thrown off through the kidneys as waste."[2]

[1] Sehste Auflage, dritter Band, 1899, p. 253.
[2] Loomis and Thompson's Medicine, vol. iii. p. 838.

The other theory supposes an inability on the part of the liver cells to properly retain the sugars after they have been formed into glycogen, that is, the glycogen is too rapidly changed into dextrose and levulose for the body's use, and is, therefore, thrown into the blood stream, there to accumulate in abnormally large amounts, with the usual results. Diabetes has been attributed to various diseases of the liver, such as atrophic cirrhosis, hypertrophic cirrhosis, pigmentary cirrhosis, and chronic fatty degeneration. So far as I am able to learn, no case of amyloid liver nor neoplasms of the liver has been held responsible for the occurrence of the diabetes.

Lesle and Marklen[1] found diabetes present in several cases in children suffering from chronic gastroenteritis, and ascribed it to faulty hepatic activity. A. Exner,[2] in the study of cholelithiasis, found sugar present in the urine in all but 1 of 40 cases examined, the sugar disappearing after operation for the removal of gallstones. Zinn and also W. Kausch have investigated this subject, and they, on the contrary, found sugar in but a limited number of such cases. The frequent occurrence of sugar in the urine in considerable quantities, incidental to gallstone colic, has engendered the belief by many authors that it is a sequel to cholelithiasis. It would appear that the occurrence of glycosuria in such cases might well be ascribed to a disturbance of the liver function subsequent to the bile stasis of gallstones.

Minkowski[3] found the glycogenic power of the liver reduced in atrophic cirrhosis, but did not find this to be the case in diseases of the liver in general. By feeding dogs as long as practicable with 3.5 c.c. to 4 c.c. of 90 per cent. alcohol in water, Rosenfeld[4] found the fat in the liver to become greatly increased, while the glycogen was diminished in amount. This indicated that the alcohol exerted an influence upon the glycogen-retaining function of the liver cells. It is not improbable that the fatty changes in the liver of these cases were primary, and that the glycogenic function was impaired as a result of this pathological condition. The glycogen store of the liver is found to be lessened in starvation, in fever, after injections of acid into the bile-ducts, in diabetes of man, and after extirpation of the pancreas in birds.[5] While it may not be demonstrated that in most diseases of the liver the glycogenic function is impaired, yet it appears likely, with a decreased number of healthy cells, we might expect a limitation of this function, and possibly glycosuria.

[1] Revue mens. des méd. de l'enf., February 1, 1901. Nothnagel's Encyclopedia of Practical Medicine, American edition.

[2] Deutsch. med. Woch., August 4, 1888. American Year Book of Medicine, 1900, p. 93.

[3] Ergebnisse der Allgemeinen Pathologie von Lubarsch und Ostertag, 1897, p. 720. Quoted from Nothnagel's Encyclopedia of Practical Medicine, American edition.

[4] Centralbl. f. inn. Med., October 20, 1900. Nothnagel's Encyclopedia of Practical Medicine, American edition.

[5] Diseases of the Liver, Pancreas, and Suprarenal Glands. Nothnagel's Encyclopedia of Practical Medicine, American edition, p. 408.

That the pancreas and liver are closely related as regards their carbohydrate function is conceded by many observers, notably by Chauveau and Kaufmann. Just what this relation is has never been established, and to my knowledge these cases are the first published as presenting an anatomical evidence of this relation. If Lépine's theory of glycolytic ferment, being elaborated by the islands of Langerhans and from there entering the blood and subsequently the tissues, be tenable, then we might explain the relation in this manner: Assuming that diseases in the liver so impair its glycogenic function that the sugar in the blood is increased, additional labor would be thrown upon the islands of Langerhans in the manufacture of an increased amount of glycolytic ferment to aid in maintaining the normal sugar content of this medium. In order to meet the increased demands thrown upon them, these interacinous cell groups of the pancreas would, of necessity, enlarge. Should they respond promptly and fully, untoward results would probably be averted. If, on the contrary, anything preventing these structures from enlarging and properly assuming their added responsibility, such, for instance, as would likely occur should their growth be impeded by an abnormal amount of fibrous tissue within or around them, we might expect the advent of glycosuria.

Could it be experimentally shown that enlargement of the islands of Langerhans resulted when the sugars of digestion and ingestion were prevented from entering the liver through the portal vein, thus throwing these products into the general circulation, we would have additional proof, I believe, of the correctness of Lépine's theory.[1] Unfortunately, however, experiments in the ligation of the portal vein have proven rapidly fatal to the animals, except geese, operated upon, and in consequence experimental work along this line is largely prohibited.

Another theory is suggested by Herter and Wakeman's[2] recent experiments with adrenalin chloride and other substances in the production of glycosuria. Glycosuria resulted when adrenalin chloride, potassium cyanide, etc., in weak solutions were painted on the surface of the pancreas. The action of these substances on other structures in determining the glycosuria can safely be excluded as being unimportant, in view of these investigators' experiments with potassium cyanide solutions particularly. That the glycogen in the liver was more rapidly converted into sugar in these experiments was abundantly proven. This rapid conversion of the glycogen in the liver to sugar has also been shown to exist in cases of human diabetes, fever, etc., as before mentioned. It seems reason-

[1] Since writing the above the discovery by O. Cohnheim that extracts from either the muscles or pancreas alone are without effect on the oxidation of glucose, but being combined destroy sugar completely, apparently gives support to Lépine's theory, in so far as glycolysis is concerned.

[2] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, January, 1903, No. 1, vol. cxxv. pp. 46–61.

able to believe that the secretion of the islands of Langerhans exerts an inhibitory influence on the cells of the liver and possibly also the muscles, preventing them from too rapidly converting their glycogen store into sugar, and that the action of the adrenalin chloride and similar substances is just the opposite, augmenting glycogen conversion. It might be argued, in so far as Herter and Wakeman's experiments are concerned, that these substances, when applied to the surface of the pancreas, in some way neutralize the action of the secretion of the islands of Langerhans, thus temporarily destroying its inhibitory influence on glycogen conversion. The idea is also suggested in man and other animals that the normal secretions of the islands of Langerhans and the adrenals are, to a certain extent, antagonistic, and that the normal secretion of the adrenal glands controls the inhibitory influence exerted by the normal secretion of the islands of Langerhans on the liver cells in the conversion of glycogen into sugar. In other words, secretions from these gland structures in normal amounts act upon each other in such a way as to establish a balance in carbohydrate metabolism. On this basis the hypertrophy of the islands of Langerhans in our cases could be explained as follows: With a limitation of the power of the liver cells to retain their glycogen, an additional secretion of the interacinous cell groups of the pancreas is called for to aid them, or the remaining uaffected liver cells, in carrying out this function. These islands respond by enlarging. The influence of the secretion of the islands of Langerhans on the liver cells may be brought about directly or indirectly through the nervous system.

In addition to the cases given above, one of exceptional interest has come to my notice. It was a case of extensive hyaline degeneration of the islands of Langerhans without diabetes. I know of no case on record in which a marked affection of this kind has been found without the occurrence of sugar in the urine. The histological picture presented by the pancreas in this case is very similar to those described by Opie, Wright and Joslin, Herzog and others.

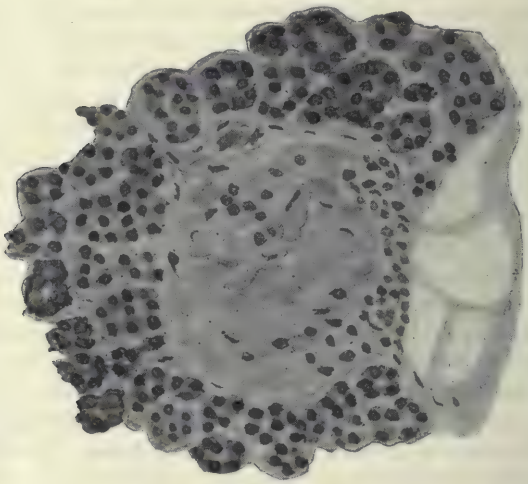
The subject of this case, a male, aged seventy-two years, was admitted to the Independence State Hospital October 30, 1901; he died August 11, 1902. While in the hospital he suffered from a chronic, suppurative mastoiditis with extensive bone necrosis, eventuating in death from extension into the lateral sinus of the side affected. Unfortunately, only two urine analyses were made; one, two days after admission; the other a little more than a week before death. The urine at both examinations was entirely negative. It seems more than likely, however, that had the patient suffered from diabetes at any time while in the hospital, sugar would have been found in his urine at these examinations, and the clinical signs of the disease have been observed. He had no symptoms of diabetes.

The anatomical diagnosis in the case is as follows: Necrosis of the mastoid process of the left temporal bone; septic thrombosis of

the left lateral sinus; double, old pleuritis; congestion of lower lobe of right lung; sclerosis of aorta; sclerosis of aortic and mitral valves; perisplenitis; perihepatitis; interstitial hepatitis; arterio-sclerotic atrophy of the kidneys with cystic degeneration; chronic cystitis.

Histology of Pancreas. Everywhere the interlobular tissue is slightly increased. The interacinous tissue is much increased in some places, having replaced or caused the atrophy of individual acini. In some sections of the pancreas, however, the fibrous tissue appears of normal amount. The islands of Langerhans are abundant and vary greatly in size; the largest island measuring 0.608 mm.; the smallest island measuring 0.057 mm.; the average measurement being 0.244 mm. Within the most of the islands of Langerhans the

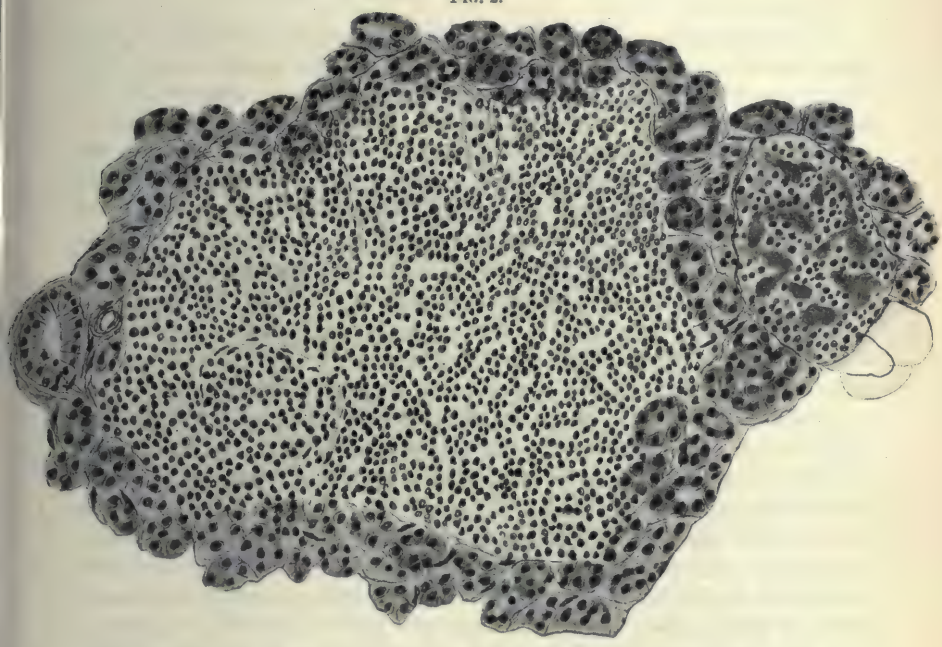
Fig. 1.



fibrous tissue appears normal. Fully four-fifths of the islands contain small isolated or large conglomerate masses of homogeneous substance, staining a bright pink with eosin, cherry-red with Van Gieson's stain, and ultramarine-blue with Mallory's aniline-blue connective-tissue stain. A few of the islands thus affected contain so little of this substance that close observation is necessary to detect it. The most of the islands, however, contain much of this hyaline material, some, in fact, being almost entirely converted into homogeneous masses, appearing not unlike fibrohyaline glomeruli in a fibroid kidney (Fig. 1). This same material is found in the lumina of some of the acini. Not infrequently a greatly affected island is found in close proximity to one entirely normal; these normal ones being, for the most part, very large; the largest island found, for instance, being entirely unaffected (Fig. 2).

The non-occurrence of diabetes in this case may be explained by the assumption that the greatly enlarged, unaffected islands of Langerhans have fully assumed the lost or limited function of the affected ones. The damaged liver may also have had some bearing upon their enlargement. This case not only illustrates that a marked hyaline degeneration of the islands of Langerhans can occur without producing glycosuria, but also furnishes additional proof of the propensity of these structures to undergo a compensatory hypertrophy. There is a possibility that sugar had at some time appeared in the urine, but had disappeared by the assumption of the healthy islands of Langerhans of the additional labor placed upon them.

Fig. 2.



Such a possibility is also suggested in those cases of diabetes in which the sugar content of the urine becomes lessened or even disappears after varying lengths of time. Furthermore, in those cases in which a cure is affected by proper dieting, the *modus operandi* may be explained in a similar way. It has been shown that if patients suffering from certain mild forms of diabetes be placed on a diet entirely free from carbohydrates, the sugar in the urine entirely disappears. Now, if the patient is fed on gradually increasing amounts of white bread along with albumin and fat until sugar begins to appear in the urine, his oxidizing capacity for sugar can easily be determined. Then, if placed on a diet somewhat poorer in carbohydrates than the one which caused the appearance of sugar

in the urine, food richer and richer in carbohydrates may gradually be given until he is able to assume his natural diet. One may assume that during the process of dieting the healthy islands of Langerhans have undergone a sufficient hypertrophy to compensate for the decrease of functional activity in the unhealthy ones.

Conclusions. 1. Diseases of the liver are generally accompanied by an enlargement of the islands of Langerhans, which is considered a true compensatory hypertrophy.

2. The fact that the liver and the islands of Langerhans have been shown to possess properties which aid in governing the carbohydrate metabolism, suggests that it is the limitation of this function in the liver which is being compensated by the enlargement of the islands of Langerhans.

3. Two theories, at least, concerning the *modus operandi* of this phenomenon, are worthy of consideration. One, based on Lépine's theory, assumes the elaboration of the glycolytic ferment in the islands of Langerhans, which, entering the blood, causes the oxidation of any sugar in excess of the normal amount, and that with an increase of the sugar in the blood resulting from hepatic disease an additional responsibility is placed upon the islands of Langerhans in the elaboration of this ferment, in order that a normal sugar balance may be established. These structures, if healthy, in response to the additional demands placed upon them, undergo hypertrophy. Another theory, suggested by Herter and Wakeman's experiments with adrenalin chloride and similar substances, is that the secretion of the islands of Langerhans possesses an inhibitory influence upon the liver cells in their property of converting glycogen into sugar, and that with a decreased liver activity an additional functional activity of these islands is stimulated, and they, in consequence, become hypertrophied.

4. It is probable that diseases of the liver occur prior to cirrhotic changes in the pancreas, as shown by certain cases in which the islands of Langerhans are greatly enlarged but otherwise unaltered, though surrounded by dense bands of fibrous tissue.

5. It is probable that an increase in the number of islands of Langerhans occurs through a transformation of the acini of the pancreas into these structures, as is seen in a certain number of cases in which the fibrous tissue of the pancreas is not increased, though an unusual abundance of interacinous cell groups are present.

6. Severe involvement of the islands of Langerhans in a hyaline degenerative process may occur without the usual resultant, diabetes. This is explained by the fact, in the one case presented, that the unaffected islands have undergone an immense hypertrophy, thus fully compensating for the lost or limited function of the affected islands.

7. The property the healthy islands of Langerhans possess of undergoing a compensatory hypertrophy explains, in some cases of

diabetes, the lessening and even the final disappearance of the sugar in the urine. This property of the healthy interacinous cell groups of the pancreas also explains the rationale of the treatment in certain mild forms of diabetes by restriction of a carbohydrate diet. The non-occurrence of sugar after return to general diet may be taken as evidence that a sufficient degree of hypertrophy has occurred in the healthy islands of Langerhans.

ORTHOSTATIC ALBUMINURIA.

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Physicians who examine large numbers of presumably healthy young adults, as do life insurance examiners and army and navy surgeons, occasionally meet with individuals showing albuminuria; careful physical examination, however, shows none of the cardiovascular changes of nephritis, and microscopic examination of the sediment is entirely negative. I have met with 5 such cases in the last five years, 4 of them having learned of their albuminuria from insurance examiners.

During the last nineteen years, ever since Pavy's[1] first report of 6 cases published in 1885 in the *Lancet*, numerous cases have been recorded in the medical literature of all countries, more especially of Germany and France. Moxon,[2] in England, as early as 1878, reported cases of intermittent and adolescent albuminuria, classifying them into two groups: those showing renal disease, and those not showing it, the latter cases being distinguished by pulses of low tension. T. M. Rooke[3] the same year reported 2 cases, aged fourteen years and sixteen years, respectively, in whom albumin constantly occurred in urine secreted and passed during the day, and in whom it was constantly absent in urine secreted and passed during the night. A similar case, reported by Clement[4] in 1881, showed disappearance of albuminuria after the patient had spent an hour or two quietly in bed. It was Pavy, however, whose paper first gave impetus to the more thorough appreciation of the subject, and he acknowledges Moxon's priority in the report of cases. Pavy reported 6 cases in his first paper, adding 3 more in a second paper the following year. Two of the original 6 cases were kept in sight for a year, 1 at the end of that time being free from albuminuria, the other still showing it. A group of 3 cases, followed for two years, recovered; one case, followed for four years, constantly showed albuminuria. The second series of 3 cases were those of two boys and one girl, the original 6 being men and boys. Pavy discovered that all

9 of his cases showed no albumin on rising, more or less at mid-day, and a trace in the afternoon, lasting till the patient retired. Fasting made no difference in the amount of albumin detected. Pavy, therefore, proposed the term "cyclic" albuminuria, a term which still remains firmly established in medical literature. That the albuminuria is not due to renal disease seemed evident to Pavy, both on account of the entire absence of cardiovascular signs of nephritis and on account of the absence of casts and other pathological findings in the microscopic examination of the urine. Stirling, in 1887, reported a case of which the upright position was constantly associated with albuminuria, and proposed the term "postural" albuminuria. Heubner, from whose service at the Charité Hospital, in Berlin, 7 cases were reported by Schön,[5] recognizing the relation between the upright position and the presence of albumin, proposed the term "orthotic" albuminuria, the albuminuria of the upright position. This term was further improved upon by Teissier (of Lyons), and Merklen, who invented the word "orthostatic" as the descriptive term for the symptom, and French writers uniformly allude to the condition to-day as "orthostatic" albuminuria. In the United States this euphonious term is prevailing, but in England and Germany Pavy's and Heubner's appellations are the more usual ones.

Attempts at classification of these numerous cases meet with failure, because of the fact that orthostatic albuminuria may be a symptom of some form of Bright's disease, notably chronic interstitial nephritis, or may be a condition *per se*. For example, a few cases of chronic interstitial nephritis may show no albumin in nocturnal urine, but may show traces in diurnal urine. Strictly speaking, orthostatic albuminuria is albuminuria from whatever cause, occurring while the patient is standing erect. It is permissible, however, to limit arbitrarily the term to those cases of orthostatic albuminuria in which, upon physical and microscopic examination, there are no signs of renal disease. If there are such signs, then Bright's disease should be diagnosticated, and the accompanying orthostatic albuminuria be alluded to as merely a more or less interesting symptom.

On attempting to classify cases of orthostatic albuminuria with normal cardiovascular systems and normal microscopic findings in the sediment of the urine, in other words, orthostatic albuminuria in the limited sense of the word, we shall find that they fall into the following classes:

1. Intermittent Cases. These cases show an albuminuria continuous for weeks or even months; then stopping for a time, only to reappear after an interval of varying length. In the course of time they seem more likely to develop into Bright's disease than the second group of cases about to be mentioned; indeed, both Bright and Gull have described typical cases of Bright's disease thus insidiously beginning. Followed a few years these cases are likely to

show casts in the urinary sediment. As to age, there are two subdivisions among the intermittent cases:

(*a*) *Adults.* The grown patients with intermittent albuminuria show no distinctive characteristics, morbid or physical.

(*b*) *Children.* The children with intermittent albuminuria are usually cases of post-infectious nephritis, diphtheria, and scarlatina, giving rise to the larger number of cases. It is not essential that the nephritis be the immediate sequel of the infection, cases being reported where an interval of several months has occurred between the time of infection and the time of appearance of the albuminuria.

2. Continuous Cases. These cases show an albuminuria which is continuous, often for years, never intermitting, and, when finally passing away, doing so never to return. Though they may be of long duration, as a rule, they are transitory. Ewald[6] and others believe that they never develop into cases of true nephritis. As to age, there are two subdivisions:

(*a*) *Adults.* Grown people affected with this sort of albuminuria are almost invariably neurasthenic. So true is this, that the introduction of the term "neurasthenic albuminuria of adults" would not be amiss. As long as the marked vasomotor paresis, so frequent a symptom of neurasthenia, persists, so long does the albumin appear in the urine. The vasomotor paresis has for its best and most reliable symptom the beating of the abdominal aorta, the degree of beating often being so pronounced that the inexperienced for the time entertain the suspicion of abdominal aneurism, the beating being due, however, merely to vasomotor paresis, with a resulting loss in the elasticity of the aortic wall.

(*b*) *Children.* Continuous orthostatic albuminuria in children in large measure is associated with movable kidney, rather than with neurasthenia. The movable kidney is undoubtedly always congenital, and, as a rule, is not associated with splanchnoptosis. Kuttner,[7] out of 62 cases of orthostatic albuminuria of all ages, reports 22 of movable kidney in children, a proportion of 35.5 per cent of all types of cases at any age. Sutherland[8] reports 15 cases of movable kidney in 40 cases of all ages and types, 37.5 per cent. of the total. Relatively, therefore, this subdivision is a large one.

Both of these general divisions of orthostatic albuminuria, the intermittent and the continuous, are "cyclic" in the sense in which Pavy used the word; that is, both show the albumin in largest amounts in the forenoon hours, in smaller amounts in the afternoon and evening hours, and both show the absence of albumin during the night. Both of these general divisions, the intermittent and the continuous, are "orthotic" or "orthostatic," since both show albumin while the body is in the standing or erect posture, and both show the absence of albumin while the body is reclining, whether during the night or during the day. It is evident from my attempts, then, at classification, exactly as Achard[9] states, that orthostatic albu-

minuria is not a nosographical type, sharply demarcated and deserving a description of its own, but is rather a symptom occurring in many different conditions. Moreover, there are cases, which, as Méry and Touchard[10] point out, are continuous during the first few years of their existence, and which subsequently metamorphose into the intermittent type. Where, then, should these cases be classified? We must admit that no hard-and-fast line of demarcation can be drawn between Group 1 and Group 2 of my classification.

Concerning the frequency of occurrence of these cases, some idea may be had from the large numbers reported. For example, Van Noorden reports 154 cases in healthy soldiers in the Netherlands army (Stokvis[11]). Zecthuisen reports 13 cases from an eye clinic. Stokvis reports the case of a superior officer in the Netherlands army in whom albuminuria was accidentally found, and who, on account of it, was kept out of service for months, being finally invalided home. He felt well, and disliked the order exceedingly, but was forced to yield. For several years he was in Stokvis' care, the albuminuria constantly persisting. Stokvis reports other cases. Heubner[5] reports 7 cases; Pavy[1], 9 cases; Edel,[12] 3 cases; Huger,[13] 2 cases. Kuttner,[7] from Ewald's clinic, gathered in ten years 62 cases; Sutherland,[8] 40 cases; Beck[14] reports 1 case; Teissier, numerous cases. In the *Bulletin et mémoires de la Société médicale des hôpitaux* for 1900 and 1901 numerous cases are reported by Teissier, Méry, Achard, Lenoissier, Lemoine, Touchard, Le Noir,[15] and others.

As to the chief etiological factors, Senator[16] states that most cases occur in adolescent girls. Of Sutherland's[8] 40 cases, 30 were females; of Le Noir's[15] 24 cases, 15 were females. On the other hand, 4 of my own cases were males. Of Pavy's 9 cases, 8 were males. Huger,[13] after a study of the literature, reports 88 per cent. of cases in males and only 12 per cent. in females. These diverse statistics may, perhaps, be reconciled, the preponderance of males occurring chiefly in the practice of those concerned in insurance or army examinations, and the preponderance of females in those with a practice in children's diseases, as in Sutherland's and Heubner's cases.

As to the age, Kuttner[7] reports as follows:

3 to 5 years	14 cases.
5 " 10 "	16 "
10 " 15 "	22 "
15 " 20 "	12 "
20 " 25 "	6 "
29 "	1 case.
32 "	1 "

Le Noir in 24 cases reports:

Under 10 years	2 cases.
10 to 20 "	10 "
20 " 30 "	5 "
Above 20 "	7 "

The maximum incidence in Kuttner's 62 cases is between the fifth and the fifteenth years, 38 of the cases, or 61 per cent., occurring at that period of life. Ewald,[6] from whose clinic Kuttner's cases were reported, agrees with Kuttner. Huger, who looked up the literature, concludes that most cases occur in adolescence, but notes that instances occur at any age. Pavy's 6 original cases occurred at the ages of eighteen, nineteen, twenty-one, twenty-eight, and forty-nine years; two at nineteen years.

Those who find a majority of cases in children naturally turn to the infectious diseases as a cause. Thus Méry and Touchard report a case in a girl aged fourteen years, following diphtheria and pertussis. Senator agrees that many cases follow the infectious diseases. Even adults may trace the albumin apparently to an infectious disease, Hertz and Salomon[17] reporting a case in a male aged twenty-three years, the albuminuria developing a few months after scarlet fever. Siredey reports a case of post-scarlatinal orthostatic albuminuria of the intermittent form in a young girl. Le Noir, who reports 24 cases of intermittent albuminuria, not necessarily orthostatic, though some of them were of that type, noted that 3 followed scarlet fever, 4 followed typhoid fever, 1 followed puerperal fever, and 5 followed smallpox.

In some cases baths have been thought to have a causal effect in the production of orthostatic albuminuria. Thus Remi Picci and Galewitch report cases apparently due to warm baths (Stokvis[11]); and Ewald[6] admits the possibility. Cold baths are also a cause, just as they are a cause of paroxysmal hæmoglobinuria. Indeed, in these cases it seems as if no hæmoglobinuria resulted, but instead a paroxysmal albuminuria. On the other hand, Edel believes that warm and even cold baths are actually curative in orthostatic albuminuria, since he believes them to promote diuresis.

Exercise and overexertion are apparently not causal factors, every author of note agreeing on this. Pavy's experiments early demonstrated that no increase of albuminuria ever resulted from overexertion. Indeed, Edel goes so far as to propose exercise as a curative measure.

Some cases are hereditary or familial. Thus Schön,[5] reporting cases from Heubner's clinic in 1895, found cases of orthostatic albuminuria in two sisters, one aged fifteen years and one aged thirteen years. Similarly, Achard[9] reports cases in sisters, a girl aged twelve years and one aged eighteen years. Le Noir reports a family consisting of five children, the older sisters showing no albumin and the three boys orthostatic albuminuria, two being twins. The mother had had albuminuria ever since she was seventeen years of age, and had passed through five pregnancies without any impairment of health whatever. Of my own cases, 2 are familial; a father and his nine-year-old daughter show orthostatic albuminuria, the only remaining child being free from it.

The ingestion of food is without influence, according to most observers, from Pavy down, Pavy noting that fasting did not reduce the albumin. Indeed, Edel believes the ingestion of food diminishes the amount of albumin present, and thinks it does so by promoting diuresis. Lenoissier and Lemoine,[18] however, noting that people eat during the day and sleep at night, illogically look upon food as a possible causal factor. Méry and Touchard, in one of their three conclusions summarizing the leading points of their paper, declare that there is an absolute absence of effect upon orthostatic albuminuria by digestive labor. Indeed, the very fact that the maximum albuminuria is before dinner, and that it decreases in the afternoon and evening, when the heavier meals are customarily taken, would seem to indicate the inadequacy of food as a causal factor.

The consensus of opinion is that the erect posture is the chief etiological factor. Concerning the influence of the erect posture in general upon the elimination of water and of urea in the urine, careful experiments by Lenoissier and Lemoine[18] are of interest. These investigators found that standing notably lowers the secretion of water by the kidneys in all individuals, whether healthy or suffering from Bright's disease. The diminution of the quantity of urine passed was found to be greater when the kidneys are diseased than in the healthy state, and the difference is sufficiently marked and sufficiently constant to indicate that excessive orthostatic oliguria is a very delicate sign of defective renal function. The most pronounced reduction that these authors found was 71 per cent. while standing; that is, 29 per cent. as much was secreted standing as lying. If one furthermore measures the excretion of urine during the period of prone posture following the erect posture, a compensatory polyuria will be found. Nevertheless, the quantity of urine secreted in twenty-four hours remains lower than the total which the patient might have secreted had he remained constantly in bed. In a series of patients the average diminution of urine passed in the erect posture was 25 per cent.

Conversely, the erect posture, both in disease of the kidneys and in health, has influence upon the elimination of urea, a greater quantity being secreted in the upright posture, a lesser quantity in the prone position. In the light of these two facts it is not difficult to appreciate the influence which the upright posture may really have upon the elimination of albumin. Moreover, the early experiments of Dukes Clement with his patient, of Pavy with his patients, and of numerous observers since, tend to establish incontrovertibly a close relationship between the upright posture and orthostatic albuminuria. Whether the upright position is the real cause, or whether it is a posture permitting the exercise of a more remote cause, is, of course, not established. That it may not be the real cause is evident from the fact that there is usually a diminution of

albuminuria toward the end of the day, after the patient has been standing the maximum time-length.

Kuttner was the first, I believe, to point out a relationship between movable kidney and albuminuria in young girls. He found the right kidney movable in 22 out of 62 cases, or in 35 per cent. In 19 of these 22 cases both kidneys were movable. Le Noir reports that of his 24 cases, 8 had movable kidneys, or 33 per cent., a figure closely agreeing with Kuttner. All 8 of his cases were females. Sutherland found in a total of 40 cases of orthostatic albuminuria in adolescence, 15 with movable right kidney, in 5 of whom both kidneys were movable. His percentage is, therefore 37.5. Adding these three sets of cases, we find 45 cases of movable kidney in 126 patients, a percentage of 35.7. The average age of Sutherland's patients was ten and a half years, the extreme variations being seven and fourteen years. Since Sutherland's total of movable kidney in the 40 cases of orthostatic albuminuria was greater than found in all the remaining patients of his hospital service during a period of fifteen years, its relationship as expressed by this fact is very important. Sutherland, however, regards the movable kidney as an effect of the orthostatic albuminuria rather than as a cause, his explanation being that the daily surcharging of the kidneys with venous blood when the patient assumes the erect posture, and the consequent increased weight of the organ, may in time tell upon the normal supports and induce a certain progressive degree of motility. Movable kidney was also reported by Bourcy,[19] in the case of a youth, aged nineteen years, and by Nivière,[20] in a young man, aged twenty years.

Pathology. Inasmuch as not a single case of orthostatic albuminuria has ever to come to post-mortem examination, there is no knowledge whatever as to either presence or absence of renal changes. There are theories of pathogenesis, to be sure, which are more or less plausible, and there is a fairly widespread idea that orthostatic albuminuria is functional or physiological. Of exact information, there is none. Senator[16] has long been of the opinion that albuminuria of the intermittent type may be physiological. According to him, physiological albuminuria exists, though limited to very small amounts of albumin, in healthy individuals of not very advanced age, in whose urine there is no evidence of any departure from the normal and in whose cases the albuminuria is called forth only by certain physiological causes, chief of which are overexertion, overeating (especially of proteids), cold baths, emotional disturbances, and mental overwork. Such cases of albuminuria must, however, be operative only in a transitory and desultory way, and cannot account for the continuous cases of orthostatic albuminuria so frequently observed. Others, and the majority of writers, are decidedly opposed to Senator's view, and, personally, I belong to the majority.

Edel,[12] observing that the amount of albumin diminishes after dinner, being less from three to six in the afternoon than in the forenoon, a fact exactly opposed to the idea that food increases the amount of albumin, sought a new explanation, which he endeavored to prove. He made the experiment of postponing the dinner hour, and discovered that he also postponed the time of minimum albuminuria in every case examined. He then abolished the dinner altogether and entirely eliminated the period of minimum albuminuria. He found, further, that, as is generally known, the ingestion of food causes increased diuresis. The recumbent posture is also associated with diuresis. He therefore arrived at the conclusion that the true theory of origin of the albumin is that it results from diminished diuresis, and hence proposes as a cure the ingestion of larger amounts of water and various diuretics. Ewald does not agree with Edel, and the latter's hypothesis has failed to attract much attention or any following.

The most plausible theory of pathogenesis is that of Marie and numerous other writers. As is suggested in my classification, it was early noted that cases of orthostatic albuminuria in young adults and even in older individuals were, as a rule, associated with hysteria, neurasthenia, and dyspepsia nervosa. In all of these individuals there was considerable vasomotor paresis indicated by the cold and semicyanotic extremities and by the beating abdominal aorta. Marie, while necessarily indefinite, subscribes to a theory of vasomotor origin. Ewald,[6] writing in Eulenburg's *Jahrbuch* upon renal diseases in the volume recently issued in January, 1904, puts the matter in this way: "When we consider all the facts that we have knowledge of concerning the genesis and causes of this peculiar affection, we are able to assert with certainty only this much: that disturbances of the circulation must be the underlying factors, manifesting themselves through the influences of certain reflexes in the renal parenchyma." The exact area is thought by Ewald to be in the glomeruli, though he admits the possibility that the tubules may also be within the area of vasomotor disturbance. As to the cause of the diurnal variations in the circulation, neither Ewald nor any other authority has been able to afford any information.

Symptomatology. *The Urine.* The quantity of urine passed in the twenty-four hours is approximately normal, averaging 1100 c.c. or 1200 c.c. in the young to 1500 c.c. or 1600 c.c. in adults. The specific gravity is not at all lowered; indeed, in a case reported by Beck,[14] the average specific gravity of 36 specimens, passed over a period of six months, was 1026.2.

The albumin found is serum albumin or globulin, best detected by the acetic acid and ferrocyanide of potassium test. Nucleoalbumin, according to Ewald, may be present, but it is very rare, The albumin is present, as a rule, in relatively small quantities, such as small or large traces, but it may be present in large amounts, even

⅛ of 1 per cent. The daily variation is fairly regular, there being no albumin in urine passed on rising, a maximum amount in that passed during the forenoon, usually about 11.30 A.M.; while in the afternoon the amount of albumin falls, reaching a minimum in the evening. In appearance the urine is perfectly normal, being lighter in color and increased in amount in the afternoon.

Microscopically, casts are rarely found. In Pavy's original paper the absence of casts was one of the diagnostic points. Personally, I was able to find casts in but 1 of my 5 cases, and I suspect that eventually cardiovascular signs of nephritis may develop in him. Ewald agrees that in the majority of true cases there are no casts. Huger,[13] reporting 2 cases of young men, both under twenty-one years, found casts in the urine of each. He expresses himself as feeling certain that very careful examination will show casts in all cases of orthostatic albuminuria.

Cryoscopy affords no information in regard to the presence of nephritis, the reduction of the freezing-point being within the normal variation. The methylene-blue test made by Hertz and Salomon also resulted negatively, indicating the probable absence of renal disease.

Subjective Symptoms. As a rule, there are no subjective symptoms in these cases, most individuals regarding themselves as healthy, still the patient may be languid, though not sick, and, according to Marie, may suffer from neuralgias of various sorts, palpitation, vertigo, and even nose-bleed. He is more apt to suffer, however, from hysteria, neurasthenia, or dyspepsia nervosa. The vasomotor disturbances are the most pronounced, cold hands and feet being the rule, and pulsatory abdominal aortas being very common. The arterial pressure is reduced in all true cases of orthostatic albuminuria. If it is found increased, the case is very likely a true nephritis, originating insidiously.

The vasomotor paresis doubtless explains the acceleration of the pulse, the variations of rate in Kuttner's 62 cases being as follows:

Rate	60	to	70	2	cases.
"	70	"	80	14	"
"	80	"	90	25	"
"	90	"	100	12	"
"	100	"	110	9	"

Thus, 46 had a pulse rate of 80 or more. Many of these cases of Kuttner were anæmic and chlorotic, and the increase in pulse rate may thus also find an explanation. In all 5 of my own cases there was an increased pulse rate.

Le Noir noted in his 24 cases that the individuals were, as a rule, thin, the deficient nutrition possibly being due to the dyspepsia and constipation which he frequently found.

Cardiovascular signs are invariably absent, there being no hypertrophy of the left ventricle, accentuation of the second aortic sound,

increase in arterial tension, as shown by the pulse and tonometer, ocular symptoms, œdema, or polyuria.

Diagnosis. The diagnosis is not difficult. Given a case of albuminuria, an examination of the urine passed by the patient on rising should be made. If this is found free from albumin, a series of samples should be collected during the next twenty-four hours and analyses made of each of them. If by this means the case shows an orthostatic albuminuria, other alterations in the urine should be sought, such as polyuria, marked oliguria, marked reduction of urea, lowered specific gravity, microscopic signs of renal diseases, such as various casts, renal epithelial cells, erythrocytes and leukocytes. These being negative, and by the previously made physical examination, the heart and bloodvessels being found free from signs of nephritis, the eyes free from hemorrhagic or albuminuric retinitis, the skin from œdema, and the nervous system from signs of renal involvement, the diagnosis of orthostatic albuminuria may provisionally be safely made. The case should then be kept under observation for many months, and repeated tests for albumin be made, so that the case may be accurately classified, either in the great group of insidiously beginning nephritis or in the group of symptomatic orthostatic albuminuria, or in the lesser group of true orthostatic albuminuria. When placed in the latter category, it must then be determined whether the case belongs to the intermittent or to the continuous type.

Prognosis. It seems very clear to all who have written on the subject that many cases of orthostatic albuminuria wholly recover. Thus, in Kuttner's 62 cases, 34 recovered within a year, 26 being followed from two to ten years. It seems equally clear that many of those not recovering do not subsequently develop into cases of nephritis. Thus Le Noir reports a case of a girl, aged eighteen years, followed until the age of thirty-two, at which time the case was reported; this girl married and went through three pregnancies without accident. She showed albumin daily, yet always remained in excellent health. Another case reported was that of a young girl, followed since she was seventeen years of age, who went through five pregnancies without mishap. Ewald is equally sure that there is no indication that the typical and undoubted cases lead to nephritis. Indeed, most cases do quite the reverse; they recover. Klemperer also states that these cases never run into Bright's disease. Teissier, of Lyons, who reported 28 cases in 1896, reported only 4 cases which subsequently developed Bright's disease; the other 24 recovered or else continued to pass albumin during the daytime without signs of nephritis developing. Lambert,[21] writing on the prognosis of albuminuria, states that the albuminuria of adolescence (seventeen to thirty years) is of good prognosis, expressing the opinion that few men pass six months of their life without casts or albumin of transient duration. Méry and Touchard report the

case of a girl with orthostatic albuminuria who married and went through a pregnancy without accident. Huger, on the other hand, finding casts in the 2 cases he reported, and believing that casts can be found with very careful search in all cases, believes them all to be latent Bright's disease. Achard[9] sensibly remarks that "in presence of a case of orthostatic albuminuria we cannot, especially before we have followed the patient for some years, formulate an unreserved prognosis."

Personally I am of the opinion that these cases showing the intermittent type of physical signs found in non-neurasthenic adults, with possibly a slight lowering of the specific gravity, even without the presence of casts, much more in their presence, should be regarded as cases of true organic renal disease. Those cases of continuous orthostatic albuminuria occurring in adults who are neurasthenic or hysteric, with unimpaired specific gravity and negative microscopic findings, should be regarded as functional in origin, with a relatively good prognosis. Those cases occurring in children, associated with movable kidney or with no apparent cause whatever, especially familial cases, should be regarded as functional, with good prognosis. Those cases occurring in children and associated with infectious diseases, as diphtheria, scarlet fever, variola, pertussis, and even typhoid fever, should be regarded as cases of true nephritis, very likely glomerular; and though they may recover, still, the prognosis should be reserved.

The amount of albumin is of no prognostic value whatever; small amounts may mean nephritis, large amounts may mean functional derangement. Of more importance from the prognostic standpoint is the manner of life of the patient: his business cares and worries, his food and the manner and regularity of getting it, the amount of alcohol he consumes, his habits with regard to tobacco, the amount of sleep he gets, etc.

I believe that with time and the multiplication of reported cases we shall come to look upon orthostatic albuminuria, first, as a symptom of beginning nephritis; second, as a functional derangement associated with vasomotor disturbance, especially in hysteria and neurasthenia, and neuropathic individuals in general; third, as a circulatory derangement in congenital floating kidney; fourth, as an hereditary, familial defect; fifth, as a delicate sign of postinfectious nephritis. Thus, there will be no disease of orthostatic albuminuria, *per se*, any more than there are at the present time diseases known as oxaluria, phosphaturia, or indicanuria.

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ADIPOSIS DOLOROSA.

WITH REPORT OF THREE CASES.[1]

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AND

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The three cases described below are examples of Dercum's disease, or adiposis dolorosa. Two of them are of the nodular form and one is of the localized diffuse form. All but one had the four cardinal features noted by Vitaud—viz., fatty tumor or tumors; pain, both spontaneous and induced in these cases; asthenia, and psychic symptoms. In Case I. the latter feature was wanting.

No disease of the thyroid gland was noted in any of these cases. Two of them used alcohol. Syphilis was not proven in any case. In one improvement took place under thyroid treatment. All were in women, as most reported cases have been. In none was hemorrhage from the mucous membranes present. Twenty-eight cases of this disease have been recorded according to Dercum and McCarthy. It must be more frequent than this number of cases would indicate, and will almost certainly be more often recognized when its characteristics become more widely known.

Of these three cases Dr. Hall saw one of the nodular variety in his private practice in September, 1902, and shortly afterward had the privilege of studying with Dr. Walbrach Case III. in the latter's service at the Denver City and County Hospital, after the diagnosis had been made by Dr. Walbrach. Case II. was examined by Drs. Fleming and Freeman, to whom the entire credit of the diagnosis

[1] Presented to the Denver City and County Society, March 1, 1904.

belongs. Dr. Hall testified as an expert regarding this case, but had no opportunity for personal examination. This is the first appearance of the disease in court to our knowledge.

Case I. (Described by Dr. Hall.)—Mrs. A., aged thirty-eight years, American, referred to me by Dr. Leonard Freeman because of stomach symptoms. She had a history of rheumatism at fourteen. One child was born twenty years ago; two miscarriages, at four and six months, since. No history nor appearance of syphilis. Complains of tiring easily.

She had symptoms of gastric hyperacidity, with much epigastric pain. The amount of HCl was estimated by Dr. H. R. McGraw to be 0.0198, the total acidity 75.

Physical examination negative as to internal organs. Reflexes normal. Urine negative. She was decidedly neurasthenic and complained greatly of pain over the right shoulder. Upon examination I found a fatty tumor one and one-half inches in diameter and one-third as high over the right deltoid muscle. It was very tender to the touch, and gave rise to much spontaneous pain. A somewhat larger tumor was present on the lower posterior surface of each thigh, equally tender, but with less spontaneous pain. Two smaller and similar tumors existed upon the trunk, but they were only slightly tender when compared with the others.

She had pads of fat over the clavicles, but without pain or tenderness. There were no signs of myxœdema.

She seemed ordinarily acute mentally, with good memory. She had used "headache tablets" freely for the pain, and probably alcohol as well.

I saw her but three times, the gastric symptoms yielding quickly to treatment. Acetanilid relieved the pain of the fatty tumors considerably, and she continued to use it until she removed to another town. I have not since heard from her.

This patient presented the fatty tumors, with tenderness and spontaneous pain and asthenia, but was without any marked psychic symptoms. The case should be classed in the nodular variety.

Case II.—Dr. Hall appeared in the District Court May 13, 1903, with Dr. Fleming, and, at his request, as an expert witness in this case. Drs. Fleming and Freeman have kindly given us permission to publish the following history, and to them is due the entire credit of the diagnosis and of this report:

"Mrs. C., aged twenty-five years, was bruised upon the right hip on October 1, 1901, by being knocked down upon the stone pavement by the pole of a hack. Two months later she was well so far as the bruises were concerned, the usual appearance of a contusion having entirely cleared up. In November, 1902, thirteen months after the injury, she was examined by Drs. Fleming and Freeman, and by other surgeons for the prosecution, because of a

suit brought against the owner of the team on account of the alleged damage to the right hip-joint.

"At this time she was fleshy, and the thighs were especially so. She had, over the right trochanter, a circular fatty tumor of the size of the palm and nearly an inch in thickness, very sensitive to pressure, and giving rise to much spontaneous pain as well. It was alleged to have appeared since time of the injury, and this allegation was apparently true. It was blackish in the centre, reddish and mottled toward the edges, with large veins upon the surface, and showing the lobulated appearance of fat. There was no heat nor other sign of acute inflammation.

"The extreme sensitiveness of the tumor was not noted in the surrounding area, although this part was hyperæsthetic. Pressure upon the heel caused a paroxysm of pain shooting upward to the tumor. The testimony showed that this condition had existed for months, confining her to bed most of the time.

"Under chloroform there was found to be no disease of the hip-joint, according to the report of the surgeons, but the leg was nearly one-half inch shorter than the left, and slightly atrophied, apparently from disuse because of pain. She was exceedingly pale and feeble, irritable, and duller mentally than formerly."

This was apparently a case of the nodular ecchymotic form of adiposis dolorosa. The shortening of the leg was not proven to be associated with the injury. It is interesting to note the presence of tumor about a year after the disappearance of the bruises, for there seems to be no evidence that the adiposis was present at the first examination by her physicians.

Hutchison and Allbutt mention the possible association of the disease with traumatism. Doubtless her limp was in part due to the pain upon movement of the affected limb, wholly apart from any possible bony change. She has certainly suffered greatly from the pain of the tumor.

Drs. Fleming and Hall testified that this trouble was apparently not one of surgical injury, but of the nodular variety of adiposis dolorosa, the black-and-blue appearance being recognized as of occasional occurrence in this disease. Bochroch and Dercum and McCarthy speak of the ease with which ecchymoses occur in painful adiposis, although we have not noted a record of the occurrence of discoloration upon a single nodular tumor. Much credit is due the reporters for their recognition of so unusual a form of the disease. The jury promptly rendered a verdict in favor of the defendant liveryman, there being no sufficient evidence that the trouble was the result of the alleged injury. No further history of this case could be obtained.

We find here the single fatty tumor, the tenderness and spontaneous pain, the asthenia, and the development of the mental dulness and irritability.

CASE III. (Reported by Dr. Walbrach.)—The following case of adiposis dolorosa came under my observation at the County Hospital November 10, 1902, and is sufficiently characteristic to merit attention. It was shown by Dr. Hall at his clinic at the Denver City and County Hospital, at a time when the "irritability and causeless quarrelling" reached almost to the border of actual insanity.

The case is that of Mrs. Ella N., aged forty-five years, married, housekeeper, American by birth, both parents dead, mother of old age, father of unknown cause. Patient had scarlet fever when a child. In later years pneumonia, rheumatism, and typhoid. Denies specific infection. No history of tuberculosis in the family.

Patient claims that the present trouble began four weeks ago with a swelling in the lower extremities, accompanied with intense pain in these regions, apparently of a neuralgic character. Owing to the mental condition of the patient it is impossible to obtain a clear, concise history in regard to the onset and further development of symptoms. She admits having used alcohol freely. On inspection we find both hips and both thighs and the regions around and below the knees to be enormously enlarged, giving the patient the appearance of excessive obesity in these parts. Close examination reveals that the enlargements consist of adipose tissue, which is very unevenly distributed.

Below the left knee it is very irregular and lumpy. The abdominal wall also contains a large amount of fatty tissue.

The patient has no unusual deposit of fat about the shoulders or arms. This disorder of nutrition, whatever the cause may be, was limited in this case to the lower extremities. The second prominent symptom is the extreme tenderness over the deposits of adipose tissue. Every slightest touch almost anywhere below the waist is attended with cries of pain. The patient also suffers from crises of pain, arising spontaneously without any external cause.

The third most prominent feature in the case consists of the psychic phenomena.

These consist of extreme irritability, and, to borrow an expression from Dercum, "a marked tendency to causeless quarrelling and even vague ideas of persecution." She was continuously quarrelling and fussing with the physicians and nurses, claiming that she was being neglected and maltreated.

A fourth symptom of great prominence was the marked asthenia. The patient, although apparently well nourished, was confined to her bed. Even sitting for a few minutes in a chair seemed to completely exhaust her. The grip of both hands was extremely weak.

Examination of the heart and lungs was negative. Slight atheromatous changes were noted in the radial arteries. Liver dulness seemed moderately diminished. A pelvic examination revealed nothing abnormal. Urine contained a moderate amount of pus, no

albumin or casts. Patient lost control of bladder at times. The right eye deviates outward since childhood. Reaction of pupils to light and accommodation was normal. Knee-jerks present, not exaggerated. No anæsthesia was found in any part of the body. No abnormality of the thyroid gland could be detected by physical examination.

The above-described accumulation of adipose tissue—pain, asthenia, and psychic phenomena—are regarded by Vitaut as the four cardinal symptoms of the disease, and this meets with the approval of Dercum. Having these four cardinal symptoms present in this case, we are justified in making the diagnosis of adiposis dolorosa. If we accept Vitaut's division of adiposis dolorosa into, first, the nodular; second, the localized diffused; and, third, the generalized diffused forms, we find that the case under discussion belongs to the second group, namely, the localized diffused form.

The patient was put on thyroid extract and iodide of potassium, this treatment being continued for about two months. At the end of this time she had improved to such an extent that she was able to be up and about, and left the hospital after having been confined to bed three months. When seen a year afterward the patient had apparently continued to improve without further treatment. She related that she had been able to do her usual household duties during that time and had been free from pain.

At the present time but five cases of adiposis dolorosa have come to autopsy, four of which are recorded by Dercum and one by Burr. In two of these the thyroid gland was enlarged and the seat of calcareous infiltration. Two others showed partial atrophy of the same gland, while in the fifth the gland was found to be normal. Three out of the five reported presented changes of the pituitary body, namely, enlargement and gliomatous degeneration in two, and adenocarcinoma in the third. The last three were the only ones of the five examined microscopically. Besides the above-mentioned changes an interstitial neuritis was found in various nerves as they passed through the fatty tissue. In one of Dercum's cases sclerotic changes in the columns of Goll were found. However, the neuritis and the degenerative changes of the thyroid and pituitary body are held by Dercum to be the most important pathological findings.

In comparing the pathology of adiposis dolorosa with that of acromegaly, one is confronted with the striking similarity of the lesions. In thirty-four autopsies of acromegaly recorded by Furnival, and mentioned by Osler, changes in the pituitary body were found in all, and in the majority either hypertrophy or neoplasm. In twenty-four cases in which it was examined the thyroid gland was normal in but five. The fact that both affections represent abnormal processes of growth, the one characterized by an increase of fatty tissue, the other chiefly of osseous tissue, and also that the

majority of the cases of each, so far reported, have occurred in females, is suggestive of the possibility of the two diseases having at least in part the same etiological factors.

Until we obtain a more exact knowledge of the function of the thyroid gland and the pituitary body in relation to growth and nutrition of the body, this question will probably remain undecided.

ANEURYSM OF THE HEART.

By Philip D. Bourland, B.S., M.D.,
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As far as I have been able to determine, but two examples of this interesting condition have been contributed to general literature by American writers during the last thirteen years, namely, the cases of Sailer[1] and Sangree.[2] Hare[3] reported a case of "Suspected Cardiac Aneurysm," but I do not know that the case ever came to autopsy.

Foreign writers reported during the same period a number of cases of the various kinds of cardiac aneurysms, to 34 of which I have reference by title. Of these, 23 are entitled "Aneurysm of the Heart," or do not refer, by title, to the precise location of the lesion. One specifies the interventricular septum; 1, aneurysmal communication between left ventricle and right auricle; 1, the internal mitral flap; 2, the apex; 2, the auricles, and 4, the left ventricle. Both American cases were of the left ventricle.

Not having access to the full reports of most of these cases, I am unable to analyze them as fully as I should like to. It may be assumed, however, that the left ventricle was affected in a large majority of those not definitely defined, and, in most instances, at or near the apex. Of 147 cases collected from the literature, 144 have this situation.

It must be remembered, in reading the ancient history of cardiac aneurysm, that no distinction was made between hypertrophy and dilatation and true aneurysm. The first differentiation was made by introducing the terms "active and passive" (Corvisart).

As late as thirty years ago, however, some writers discussed aneurysm and other forms of enlargement together, and without making any definite distinctions.

The case herewith reported occurred in the practice of Dr. A. A.

[1] Heart with Two Ventricular Aneurysms, Proceedings of the Pathological Society of Philadelphia, 1897.

[2] A Case of Aneurysm of the Left Ventricle, Journal of American Medical Association, 1898.

[3] A Case of Suspected Cardiac Aneurysm, Medical News, 1897.

Davis, of Calumet, Michigan, who kindly furnished me the clinical history, and at whose invitation I conducted the autopsy.

The patient, Mr. W., aged seventy-two years, had severe angina pectoris in 1894. How many attacks not stated. No previous history obtained.

In September, 1899, he had a left-sided dry pleurisy. The anterior part of the pleura was especially involved. There was much pain about the apex of the heart and little or none elsewhere. Mild fever was noted, which persisted for four or five days, after which the temperature fell to normal and the pleuritic pain gradually subsided. The patient was left in a weak and depressed state. The pulse, which, according to the patient's statement, had been more or less intermittent for some years, skipped, on an average, only once in fifteen beats at this time. The pulse rate was 75. The right radial pulse was much smaller than the left. Relative heart dulness was considerably increased, but absolute dulness was only slightly increased downward. Situation of apex beat not stated.

After about ten days periods of dyspnœa set in, attributed by the patient to flatulence. In spite of a strong though occasionally intermittent pulse, dyspnœa gradually became more severe. There was no cardiac murmur at this time. Early in December a distinct systolic murmur was first heard at the apex.

Toward the middle of December dyspnœa subsided, the murmur was no longer heard, and the appetite and strength increased considerably. After two weeks of comparative comfort dyspnœa and the murmur reappeared and the legs became œdematous. There was also œdema of the right hand and forearm, but not of the left. Dyspnœa gradually became urgent; the patient developed a short cough, expectorated a good deal of tenacious, blood-streaked mucus, and finally died on February 5, 1900, with the usual symptoms of incompensation.

The urine was negative throughout. The angina recurred once or twice at the outset of the last illness.

Post-mortem examination was made about six hours after death. The findings were as follows:

Body of medium size; muscles flabby; emaciation marked; skin sallow and dry. There is moderate hypostasis of dependent parts; marked œdema of both legs, extending well up into the thighs; moderate œdema of right hand and forearm; no œdema of left hand or forearm. Abdomen moderately distended; rigor mortis present. The head was not opened, and the spinal cord not examined.

Thorax. There are numerous adhesions between the sternum and the left parietal pleura. The pericardium and pleura are adherent, the adhesion involving a large part of the surface of the pericardium, which is distended with fluid. On opening the pericardium 200 c.c. of blood-stained fluid were removed. The pericardium is smooth and somewhat thickened; no adhesions between layers

except over lower third of left ventricle, where they are firmly adherent over an area having a diameter of two and a half inches. The heart is much enlarged; it is about twice as large as the fist; apex in sixth intercostal space half an inch inside nipple line. The left ventricle lies anteriorly, occupying the position normally held by the right ventricle. The whole heart has undergone partial forward rotation on its long axis. At the site of the adhesion between the pleura and the pericardial layers the wall of the left ventricle bulges, forming a pouch as large as a small orange. The heart with the attached pericardium was removed. It was full of dark-red fluid blood.

The Coronary Arteries. The coronary arteries are stiff and tortuous. The left coronary contains, in the auriculoventricular groove, a number of extensive areas of calcification which greatly narrow its lumen. In the anterior descending branch of the left coronary there is marked endarteritis with calcareous deposits, and nearly complete stenosis at a point one inch below the interventricular groove. The lumen of the artery narrows progressively until at the edge of the aneurysmal pouch there is practically complete stenosis. The intima and media can be easily stripped off, as a separate tube, the whole length of the vessel. The large trunk of the descending branch leading to the apex is markedly sclerosed throughout its entire length, and is completely stenosed midway in its course. There is nearly complete stenosis in the posterior interventricular branch of the right coronary. Beyond the stenosis the lumen can be traced only with great difficulty. The intima and media strip off as stiff tubes the whole length of the artery.

Section of the Heart. The wall of the left ventricle is from 12 to 14 mm. thick except in the aneurysm, where it is only from 2 to 3 mm. The muscle is pale, light brown, soft, and flabby. There is marked increase of subpericardial fat. Muscle is entirely lacking in the wall of the aneurysm, which consists of tough, fibrous tissue. The aneurysm contains a mixed clot, adherent to its wall, and merging into a red clot as the lumen of the ventricle is approached. Thorough organization has taken place in the periphery of the mixed clot, and has firmly blended it with the wall of the aneurysm. There are no clots elsewhere in the ventricle, and the endocardium is pale and smooth. The edges of the mitral segments are somewhat nodular, and there is slight curling. The orifice admits four fingers. The columnæ carneæ are flabby and flat. The right ventricle is small, its endocardium is pale and smooth, it contains blood, and its tip reaches only to within 4 cm. of the apex. The tricuspid segments are normal; the orifice admits three fingers.

The Auricles. Both auricles are dilated and thin walled, and contain fluid blood.

The Left Lung. The pleural surfaces are almost completely adherent. There is also extensive adhesion between the parietal

pleura and pericardium, involving a large part of the latter. The lung is very œdematous, but crepitates throughout. It is otherwise negative.

The Right Lung. The right pleural cavity contains several litres of blood-stained fluid. Excepting marked œdema, the lung is negative.

The Liver. The liver shows fatty degeneration and œdema, otherwise it is negative.

The Spleen. The spleen is œdematous, dark purple, and has two white, thickened patches, about one-third inch in diameter, on its anterior surface.

The Kidneys. Except for œdema the kidneys are negative on macroscopic examination.

The intestines are negative.

The Arterial and Venous Systems. The aorta contains a few yellowish, subintimal patches below the arch. The lumen is large and the walls somewhat stiffened. The aortic and pulmonary semilunars are negative. The arterial system shows, in general, only a mild grade of sclerosis. No microscopic examination was possible owing to the tissue being accidentally destroyed while in preparation.

Diagnosis. Chronic adhesive pleurisy of left pleura; chronic adhesive pericarditis; chronic fibrous myocarditis; advanced end-arteritis of coronary arteries, causing nearly complete stenosis at various points; aneurysm of left ventricle; relative insufficiency of mitral valve; moderate fatty degeneration of the liver; hydrothorax; hydropericardium; œdema of the lungs, spleen, liver, and kidneys.

In general this case presents the features common to most cardiac aneurysms. Their situation in the left ventricle, near the apex, is the rule. As to the causes leading up to the aneurysm, the obliterated, or nearly obliterated, coronary arteries and consequent anæmia, degeneration and replacement by fibrous tissue of the heart muscle, and the adhesions between visceral and parietal pericardium and pleura at the site of the infarct, with resultant traction upon the weakened heart wall, show very clearly its origin and development.

A very remarkable feature, however, is the rotation of the heart on its long axis, which threw the left ventricle forward nearly into the position of the right ventricle. I am positive that this was not the result of manipulation in removing the sternum, as the latter was very carefully raised and its adhesions with the pleura cut and not torn. It was probably caused by gradual contraction of the extensive adhesions between the pericardial and pleural layers, the latter being in turn securely adherent to the sternum, which was a fixed point from which to exert traction. Also, the suction normally exerted upon the ventricle by the lung, may be supposed to have exerted a forward pull by means of the adhesions.

Of how long-standing was the aneurysm? The development is usually slow, though rapid growth is a recognized possibility. The endarteritis of the coronary vessels was probably a slowly progressive disease, and the degenerative changes in the heart muscle doubtless proceeded *pari passu* with it. Granting that aneurysms tend to fill themselves by clot formation and organization, it may be argued, from the thinness of the pouch, that the lesion was comparatively recent. Clot formation is, however, favored by stagnation, and hence would be most rapid in an aneurysm with a constricted orifice, which was not true of this case. All things considered, one is justified, I think, in selecting the attacks of angina pectoris in 1894 and 1895 as the approximate starting point rather than the condition diagnosed as pleurisy in September, 1899.

In view of the extensive and extreme disease of the coronary arteries, the vessels of Thebesius must have been the principal contributors to the nutrition of the myocardium for some time before death.

The case adds nothing to the diagnosis of cardiac aneurysm, the symptoms having been throughout those of chronic fibrous myocarditis.

ŒSOPHAGEAL NEUROSES.

By A. L. Benedict, A.M., M.D.,
of Buffalo, N. Y.

Neuroses in general are classified under three heads: motion, secretion, and sensation. As the œsophagus has no true glands and no secretion aside from that of mucus, secretory neuroses are out of the question, unless we accept the possibility of a mucous neurosis analogous to that of the colon. Personally, I deny absolutely the neurotic etiology of a flow of mucus from the colon, believing that the advocates of this theory have put the cart before the horse, and that the neurotic condition is the result of the chronic colitis (often including a typhlitis or scolecitis) or of an antecedent splanchnoptosis, or other cause. However, if one admits a mucous neurosis of the colon, he can easily find the same thing in the œsophagus, and it is surprising that this opportunity for fame has been neglected.

Sensory neuroses, in general, are either neuralgic or are due to ordinary physiological conveyance of more or less painful sensations, or are the local expression of various organic nervous diseases, such as neuritis, tabes, and many others. There is no appreciable diminution of nervous sensibility below the nearly zero normal to internal organs, so that we cannot classify sensory neuroses as exalted and

depressed, as we can sensory and motor disorders. However, as a matter of convenience, we may recognize neuralgia, rheumatic and, theoretically, neuritic and tabetic pain in the œsophagus, as well as that due to organic lesion and the burning due to regurgitation of acrid gastric contents. It is absurd, however, to call such local pains neuroses. On the contrary, there would be a neurosis if such adequate causes of pain did not produce it. A more or less complete absence of œsophageal sensibility may occur in various paralyses and central nervous diseases.

We may therefore limit the discussion to motor neuroses. These may be classified as follows:

- 1. Depressed . . . . . .
  - Paresis (sluggishness).
  - Paralysis.
- 2. Exalted . . . . . .
  - Simple increase of peristalsis.
  - Spasm
    - Clonic
      - Direct.
      - Reversed.
    - Tonic.

Sluggishness, paralysis, and simple increase of peristalsis may be termed, after the analogy of gastric disorders, hypotony, atony, and hypertony, respectively. Or we may substitute -kinesis (with the accent on the second syllable, not rhyming with émesis) for -tony. Absolute atony or paralysis is exceedingly rare, if ever present, on account of the joint sympathetic and pneumogastric innervation of the œsophagus. Hypotony, or, as ordinarily termed, atony, is an exceedingly common condition. It may be determined by noting the delay of the œsophageal murmur after the rise of the thyroid cartilage, in drinking, and is usually associated with gastric hypotony and constipation due to intestinal hypotony. It is rather doubtful whether all these conditions should not be considered as essentially organic, on account of defective development of muscle, connective tissue and nerve fibre. At any rate, hypotony is liable to develop into dilatation, whether of œsophagus, stomach, or intestine.

Œsophageal hypertony is diagnosticated with some difficulty, or, rather, the modest clinician hesitates to adopt an arbitrary period for the passage of the bolus through the œsophagus and to use the term hypertony, if the period is accelerated by a few seconds. One must not carry the antithesis between hypotony and hypertony to the degree of assuming that œsophageal hypertony necessarily occurs in conjunction with rapid emptying of the stomach into the bowel, or through the œsophagus, or with diarrhœa. The first is more likely to be due to pyloric relaxation than to general gastric hypertony, and diarrhœa is very rarely a pure motor phenomenon, even after the ingestion of a drug.

Spasms of the œsophagus may, theoretically, be divided into those of circular, longitudinal, and both sets of muscle, but this classification is not warranted clinically. Clonic spasm, whether

direct or reversed, occurs mainly in connection with similar spasms elsewhere, especially of the stomach during vomiting. Again, a spasm typically occurring tonically may be interrupted so as to merge into a clonic spasm.

Tonic spasm, including an apparently clonic spasm due to interruption, may be stationary in one segment of the œsophagus, or may apparently travel up and down, or may change from one location to another, on the recurrence of the spasm. There is, of course, no possibility of relative movement of a fixed spasm, as in the case of spasm of a segment of intestine.

Tonic spasm of the œsophagus usually assumes one of two forms: either a dysphagia analogous to that of organic stricture, and presenting the same signs on sounding, except that the spasm may be "tired" by steady pressure, when it will gradually or suddenly relax; or the spasm may take the form of a moving globus (hystericus?). In the former case the patient complains merely of difficulty in swallowing, more or less intermittent and variously described in subjective or objective terms. It is almost never sufficient to interfere materially with nourishment, although it may occur in persons, especially young women, who are already badly nourished. There is not usually any confusion of description with that of globus. Indeed, usually the location is fixed quite definitely by the patient and is verified by sounding, and the position does not change from one time to another. Some authorities have made very definite statements regarding the location of the spasm, but my own experience allows only the statement that it is most frequent opposite the larynx, where there is a mechanical reason for spasm, and close to the cardia, where more or less of a sphincteric action is possible. At both of these levels, too, there is a fixed point of resistance. It has frequently occurred to me, as doubtless to others, to surmise that there may be an organic cause for a definitely fixed spasm, occurring in a non-hysterical individual. It is practically impossible to demonstrate, but it is plausible to assume a minute traumatism, as from a fish-bone, seed, or some similar cause.

Occasionally tonic but more frequently clonic spasm is due to some well-defined reflex cause, at a greater or less distance. The most frequent of these are regurgitation of acid chyme through the cardia; lodgement of a foreign body in a tonsillar crypt; inflammatory or other lesion of the dorsum of the tongue, fauces, epiglottis, etc.

Patient No. 54, of 1896–7, presented a rather obstinate but clearly spastic stricture of the œsophagus, several centimetres above the cardia. Some months after its relief, which was accomplished by sounding, he died of cancer at the cardia, which had been free from obstruction at the time of the spasmodic stricture.

Patient No. 43, of 1898–9, had considerable dysphagia and ischochymia, due to reflex from small tumors at the cardia and pylorus, respectively. The tumors were seen at operation and

were unable to produce mechanical obstruction at either site. The tumors were thought to be cancerous, but the patient recovered after the establishment of a jejunal fistula for a month, and she is still alive and was in excellent health when last seen.

I may digress for a moment to express the opinion that spasm of a muscular tube of the body usually indicates some real irritant, as a foreign body, calculus, painful lesion, as a small ulcer, or else that it is a reflex indication of genuine disease situated at a distance, but in the same tract. For instance, biliary spasm and jaundice may be due to scolecitis; appendicular or cæcal colic to gallstones in the biliary tract; intestinal spasm to scolecitis; gastric spasm to gallstones, intestinal worms, etc.

One of the most interesting hysterical spasms of the œsophagus that I have seen was in patient No. 67, of 1897–8, a young woman who had nursed her mother through a fatal case of cancer of the cardia. The girl simply duplicated her mother's symptoms, and there was a genuine resistance to the sound a little above the cardia. There were no other symptoms of hysteria.

Œsophageal spasm of the globus type presents many difficulties of explanation. I have seen it so seldom in ordinary hysterical cases (which do not often reach a specialist unless in nervous diseases), and so often in patients who were otherwise not in the least hysterical, that I hesitate to qualify it as globus hystericus. Is the globus purely a subjective sensation, or is there a real "lump in the throat," formed by muscular spasm and resembling that which forms at the base of a dog's penis during intercourse? When the patient describes the lump as rising or sinking gradually, is the motion purely subjective, or does the contracted area actually move? If stationary spasms are accurately located, is it not reasonable to suppose that the globus actually moves, as it seems to? Then, again, when a sober, middle-aged man of phlegmatic type describes a globus among his symptoms, why should we consider it any more hysterical than a gastric spasm causing ischochymia, or spastic constipation, or even biliary spasm?

As it had never been convenient for me to pass a sound during an attack of globus, I could not state whether a spasm was really present nor whether it really moved. Several of my friends, called by telephone, could not enlighten me. The text-books at hand did not afford any definite information. Dunglison mentions globus as a sensation. The late A. L. Loomis refers to it as the imagination of a lump rising from the epigastrium to the mouth. Frank Baker and G. L. Watson speak of it as a constriction of the muscles of the pharynx, the latter including the œsophagus. Ewald and Hemmeter omit all reference to it except as a name. G. R. Butler and James Tyson speak of it as a sensation. H. R. Hopkins informs me of his personal belief that the condition has never been scientifically studied.

One form of globus, which is quite different from an hysterical manifestation in the ordinary sense, occurs after prolonged sobbing, laughing, violent hawking to remove mucus, or even after deglutition of dry foods. This is especially likely to come on if the attempt is made to stop laughing or sobbing suddenly by swallowing or by forced inhibition. Even one or two attempts at swallowing may bring it on if the throat is already dry from dust, smoke, etc. This form of globus is almost or quite confined to the pharynx and may be succeeded by a distinct lameness.

The following table, originally published in the *Medical Fortnightly*, affords a general conspectus of the various reflexes in which the pharynx and œsophagus may be concerned more or less directly. It is unnecessary to enter into details.

Reflexes Mainly Due to the Pneumogastric Nerves.

The pneumogastrics are concerned in a number of reflex phenomena, whose function is especially to protect the respiratory and alimentary passages from injury. Such protective acts are, obviously, expulsive and depend mainly on the action of the diaphragm, whether to empty the respiratory or alimentary passages. It is convenient to consider with these protective, expulsive (and, therefore, expiratory) reflexes certain others that are mainly inspiratory. The normal ingestive processes of respiration and deglutition have already been considered.

	Expiratory reflexes.	Inspiratory reflexes.	
Primary protective	Vomiting	Swallowing	Respiratory.
Abortive vomiting	Retching		
	Gagging		
	Puking	Air-swallowing	
Abnormal, but of frequent occurrence	Belching		
	Water-brash		
	Rumination		
Laryngeal construction	Cough	Hiccough	Alimentary.
Nasal obstruction	Sneeze	Sniff	
Audible vibration of oropharyngeal cavity	Laugh	Sob	
	Crying is laugh or sob plus lacrymation.		
Laryngeal obstruction prolonged	Strain		
Prolonged inspiration with general flexor spasm	.....	Yawn	

Both inspiratory and expiratory—(single) sigh; (repeated) panting.

The various conditions included under the term aerophagia deserve our consideration. Generally speaking, aerophagia, or, rather, the subsequent expulsion of air, is construed as the formation of gas by fermentation in the stomach. Some have even gone so far as to consider it as gastric respiration, with elimination of CO_2, as in the case of the lungs. One look at a section of gastric mucosa is sufficient evidence that no appreciable quantity of gas can be formed

in this way. I have also described, in *International Clinics*, a rare method of production of CO_2 without marked fermentation, due to the union of acid gastric contents and alkaline carbonates in the upper intestine, with relaxed pylorus, so as to allow expulsion upward.

Air-swallowing is an inevitable accompaniment of ordinary deglutition and is increased by rapid eating and by certain formations of the throat not well understood. Thus there is very frequently a moderate belching of air during or shortly after a meal.

Aerophagia, as a neurosis, means almost any gradation between air-swallowing in the literal sense and a hiccough. At the former extreme the patient simply has a trick of swallowing air and belching it up; at the latter, the œsophagus is relaxed and at the sudden stoppage of the entrance of air into the larynx, by the closure of the glottis, the chest, still expanding, draws a little air into the œsophagus. In typical aerophagia there is little to justify the derivation of the word, but the condition is an hysterically magnified hiccough.

Patients No. 47, of 1902–3, and No. 64, of the same year, illustrated this condition, the latter in an exaggerated degree. The former was really a sensible, middle-aged woman, who readily co-operated in treatment, which is necessarily partly an exercise of will power. The latter patient was an extremely neurotic woman aged thirty years. She had suffered with "belching of gas" for years and would have an attack whenever excited by any cause, even the arrival of visitors. She often had attacks on the street, and rarely failed to have one when she came to my office. Sometimes they would continue for an hour or more, but at the office they were always speedily terminated by some form of instrumentation. While it was not feasible to measure the air, it was shown, by collecting it in mouthfuls, to amount to at least 100 c.c., and by blocking the mouth and nose it was clearly shown to be drawn in immediately before it was belched out. This observation was also confirmed by auscultation. It is rather questionable whether the air enters the stomach in these cases or not. Probably there is an individual variation as well as a temporary one. This neurosis is disgustingly noisy and causes much embarrassment to the patient and her family. In this particular case the patient's nose was obstructed by a mass of polyps, and it was thought that this might have had a bearing on the etiology. Its removal has not, however, produced any relief of the neurosis after a year. It is, of course, useless to treat such patients with antiseptics, unless an indication also exists in the stomach and bowels. Nerve sedatives are of some value, but the principal reliance is to be placed on instrumentation to break up spasm (as, indeed, in most forms of œsophageal neurosis), and on obtaining the patient's intelligent co-operation.

REVIEWS.

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D.; assisted by H. R. M. LANDIS, M. D. Vol. I., 1904. Surgery of the Head, Neck, and Thorax; Infectious Diseases, Including Acute Rheumatism, Croupous Pneumonia, and Influenza; Diseases of Children; Laryngology and Rhinology; Otology. Philadelphia and New York: Lea Brothers & Co., 1904.

THE March issue of this important periodical contains some of the most important sections which appear in the course of the year. The first is that by Dr. Charles H. Frazier on Surgery of the Head, Neck, and Thorax. This large field is most successfully covered, and all the real advances in diagnosis and treatment commented upon.

The section on Infectious Diseases, which includes Rheumatism, Pneumonia, and Influenza, is by Dr. Robert B. Preble. Its value is greatly enhanced by the manner in which the editor has winnowed the wheat from the straw, and extracted from the vast mass of recent literature upon these subjects all which may be accounted of real value.

Dr. Floyd M. Crandall contributes a most interesting section on the Diseases of Children, and the concluding sections, that of Laryngology and Rhinology, by Dr. Charles P. Grayson, and that by Dr. Robert L. Randolph, on Otology, cover their several specialties in a most thorough and interesting manner.

Progressive Medicine has always occupied a very different and much higher plane than all publications attempted in a similar manner. It is not a mere compilation of abstracts from the current literature, but a thorough presentation of the views of its editorial staff, which is composed of men of recognized standing in the medical profession, upon the progress of medicine and surgery, and of the various specialties. To the general practitioner or specialist it possesses great value as a progressive text-book of all the various branches of medical science.

With this volume *Progressive Medicine* appears in a new dress, which will undoubtedly commend itself to its readers. It has long been a matter of wonder with men of the medical profession in this

country that American book publishers do not issue at least some of their works in the strong paper bindings which are so commonly used in France and Germany. Such a form of publication cheapens the cost of the work, makes it much more light and convenient to hold, and permits of binding up in styles to suit the individual taste. The publishers of *Progressive Medicine* are to be congratulated upon the forward step they have taken in bringing it out in the Continental manner, and we trust the change will be appreciated by its large circle of readers. J. H. G.

American Text-book of Surgery for Practitioners and Students. Edited by William W. Keen, M.D., LL.D., F.R.C.S. (Hon.), and J. William White, M.D., Ph.D. Fourth edition, thoroughly revised and enlarged. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

In a review of the fourth edition of this book it is unnecessary to do more than comment upon the changes and additions, since its previous editions have caused it to be well known throughout the medical world as an excellent and reliable text-book. It has been brought thoroughly up to date by the introduction of the latest important contributions to surgery. We are glad to see the omission of old illustrations and their places taken up by newer and better ones. Extensive changes have been made in the portions of the book dealing with Surgical Bacteriology, Tumors, Surgery of the Nerves, etc. Five new chapters have been added to the work, which were written by well-known authorities. They deal with Military Surgery, Naval Surgery, Tropical Surgery, Examination of the Blood, and Immunity. These chapters appear at the close of the volume and are published in smaller type in order not to enlarge the book. Although the reading matter has been greatly increased, the size of the book has also been kept down by the use of a thinner paper than was employed in the former editions.

The book will continue to keep its place among the leading single-volume text-books. J. H. G.

The Treatment of Neurasthenia. By A. Proust and Gilbert Ballet. Translated by Peter Campbell Smith. New York: Edward R. Pelton.

It would seem to be a presumptuous undertaking to discuss so large a subject as the treatment of neurasthenia in a small volume of less than 200 pages, some part of which is devoted to etiology,

symptomatology, and diagnosis. By systematic classification the task has, however, been very creditably accomplished. Perhaps the subject is made to appear too simple; but what the book may lack in exhaustiveness it makes up in practical usefulness. Among the exciting causes the authors rightly dwell on the pernicious effects of worry as against the popular notion of overwork, and this applies to all classes of patients of all ages. Work alone is injurious only in the rarest cases.

The discussion of the dyspeptic symptoms occupies a large share of the authors' attention. They do not go so far as to say that indigestion is the chief cause of neurasthenia (indeed the treatment of the entire subject is carried out on the broadest lines), but rightly accord to it a prominent place in the etiology and regard it as one of the most important therapeutic indications. The Weir Mitchell system, to which a special chapter is devoted, is not advocated indiscriminately; in fact the American attitude toward neurasthenia comes in for its meed of criticism as well as of praise at the authors' hands. Rather more stress is laid on hydrotherapeutic treatment, the cold shower-bath being their measure of election. R. M. G.

A Manual of Medicine. Vol. V. Diseases of the Digestive System and of the Liver, Diseases of the Peritoneum and of the Abdomen, Diseases of the Kidneys, Diseases of the Ductless Glands. Edited by W. H. Allchin. New York and London: The Macmillan Company, 1904.

This volume comprises the diseases of the digestive system and of the liver, diseases of the peritoneum and of the vessels of the abdomen, diseases of the kidneys, and diseases of the ductless glands. The greater part is devoted to diseases of the stomach and intestine, and while the introductory general portion might have been considerably condensed without much loss to the value of the work, the clinical portion suffers from the opposite fault. From the classification of diseases of the stomach it would appear that all the functional gastric disturbances known to medicine come under the general head of gastritis. We look in vain for a satisfactory exposition of the various secretory disturbances or gastric neuroses and the methods of managing such cases. While the article dealing with physical examination of the abdomen and the analysis of gastric contents is excellent in itself, the data obtained by the examinations do not appear to be utilized in the discussion of clinical aspects of disease; the article is so imperfectly correlated with the remaining chapters on the subject as to appear almost wasted. But this is a not uncommon defect in works of composite authorship. The best portions

are those devoted to symptomatology and diagnosis; in fact, while the book is excellent for general reading, it is hardly comprehensive enough for a reference work, not even for practical matters. There is no general discussion of the indications for newer methods of treatment, about which the reader is likely to want information. You will look in vain for information on such points as the use of lavage, the indications for acids and alkalies, or the dosage of hydrochloric acid in the treatment of gastric cases. The writers have apparently ignored most of the recent work in this field.

The greatest conservatism is observed in the chapter on the diseases of the kidneys, although so much work has recently been done in an effort to clear up the classification of diseases of the kidneys and bring clinical varieties into some sort of accord with the pathological findings. The term "nephritis" is used to describe active congestion, and for all other forms of renal inflammation the terms "Bright's disease," acute and chronic, and "granular kidney" appear all sufficient to the authors. Although the title-page bears the date of the present year of grace, there is no mention, for instance, of the question of surgical treatment for diseases of the kidney, that until the present era of rapid advance in surgery were entirely given over to the medical man. On the whole, the present volume is disappointing; it is good so far as it goes, but it does not go far enough. R. M. G.

Les Nerfes du Cœur chez les Tabetiques (Etude Clinique et Anatomo-pathologique). Par le Dr. Jean Heitz, ancien interne des Hôpitaux de Paris. G. Steinheil, editeur, Paris, 1903.

The first part of this thesis gives an account of what is actually known about the cardiac plexus, including the anatomy, histology, organization of the neurones in the pneumogastric nerve, the sympathetic and cardiac plexus, properly speaking. Later, the physiology of the cardiac plexus is discussed with special reference to the sensory fibres. The second part of the treatise reviews and completes all that has been written on the cardiac symptomatology of tabetics. Aortitis, disturbance of cardiac rhythm and cardiac pains are separately considered. Then follow the results of histological examinations of the pneumogastric, sympathetic, and cardiac plexus. This work was done in the laboratories of Dejerine and Merklen. In the majority of cases there is a rarefaction of the medullated fibres in the bundles of the cardiac plexus—a lesion that is comparable to the alterations in the posterior columns of the cervical enlargement. There does not exist any relation between the lesions of the plexus and tabetic aortitis, which is essentially of

syphilitic origin. But the peculiar latency of this aortitis is account for by the lesions of the cardiac plexus and the posterior columns of the cervical enlargement. The cardiac crises probably depend upon lesions of the coronary arteries. The pneumogastric nerves are altered in about one-quarter of the cases of tabes. These lesions are manifested by laryngeal disturbances, tachycardia, and in certain cases by a marked slowing of the respiration. W. T. L.

THE AMERICAN YEAR-BOOK OF MEDICINE AND SURGERY FOR 1904. A Yearly Digest of Scientific Progress and Authoritative Opinion in all Branches of Medicine and Surgery, drawn from Journals, Monographs, and Text-books of the Leading American and Foreign Authors and Investigators. Edited by GEORGE M. GOULD, A.M., M.D. In two volumes. Vol. I., including General Medicine. Vol. II., General Surgery. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

THE *American Year-book* hardly needs an elaborate introduction to the profession. Throughout the years in which it has been published it has maintained the very highest position as a standard encyclopedia of medical and surgical progress. Dr. Gould has associated with him a staff of men of the greatest ability, and their work is marked by a conscientious thoroughness which is often lacking in writings made up from abstracts in current literature. The book is in two volumes, and constitutes a standard work of reference which should be in the library of every medical man who wishes to keep up to date in his profession. F. R. P.

THE LYMPHATICS. General Anatomy of the Lymphatics. By DELAMERE. Special Study of the Lymphatics in Different Parts of the Body. By POIRIER and CUNEO. Authorized English edition. Translated by CECIL H. LEAF. With 117 illustrations and diagrams. Chicago: W. T. Keener & Co., 1904.

A GOOD treatise upon the lymphatics is greatly to be desired, for an accurate study of the subject is, among other things, of practical value. The present volume is essentially good. It is divided into two parts. The first part takes up the subject of the lymph, the leukocytes, the development of the lymph vessels and lymph glands, and the histology of the adult structures. A short historical résumé precedes each discussion, and an extensive bibliography

is appended to each chapter. The conclusions regarding the origin and structure of the lymph vessels agree with the results of the latest researches on this subject, but it is probable that in a future edition the recent work of Sabine will be used to advantage in the chapter dealing with the origin of the lymph glands and lymph heart.

The second part deals with the distribution and arrangement of the lymph vessels and glandular groups. Each glandular group and its accessory lymph vessels is considered separately, while reference is often made to the course of metastases from malignant growths affecting different organs arising in various parts of the body. The numerous plates and drawings form a valuable addition to the text. The author's many researches upon the anatomy of the lymphatic system stamp the book with a certain degree of individuality.

The translation, though generally satisfactory, occasionally lacks clearness, as in the first part of the book, where some of the French is too patently anglicized. The volume is well printed on good paper, and is distinctly to be recommended. W. T. L.

A Manual of Fever Nursing. By Reynold Webb Wilcox, M.A., M.D., LL.D. Philadelphia: P. Blakiston's Son & Co., 1904.

The work consists of the course of lectures delivered by Dr. Wilcox to the nurses in St. Mark's Hospital.

The question of just how much to include and how much to omit in instruction to nurses on medical subjects is one that is always difficult to decide, and is best gauged by the success of the nurses who have taken the course. The author devotes the first four chapters to a consideration of fever from the physiological point of view; considers also the various types, methods of recording symptoms, diagnosis, methods of taking and registering temperatures, the taking of pulse and respiration, and a study of temperature charts. Chapter III. is devoted to general and special treatment, diet during fever and in convalescence, and is followed by a chapter full of valuable advice in regard to the hygiene of the sick room, the conduct of the nurse, and disinfection in general. In the remaining chapters the author takes up the special description of each disease to be considered, and divides the work into several classifications, namely: Infections of Continued Type; Infections of Continued Type with Local Manifestations; Infections of Intermittent Type; the Exanthemata and Thermic Fever. Here and there in the text are distributed temperature charts illustrating special types of fever.

The author's description of mountain fever is of interest as being opposed to the views expressed in the majority of recent text-books, where the disease is commonly described as identical with typhoid fever, being, however, modified by high altitude. Dr. Wilcox speaks of it as a disease caused by an organism resembling malaria, which is injected into the body by the bite of a tick. This disease is characterized by recurrent chills, by a typical eruption, by a continued fever of two weeks' duration, usually by jaundice, and is followed by desquamation and the slow disappearance of the spots, and sometimes by gangrene of the skin over the elbows, toes, fingers, or scrotum. Harvey Reed and Woodring, who have treated many cases, are both of the opinion that mountain fever is not identical with typhoid, but the disease as described by them resembles rather typhoid than that portrayed in this work. This book should prove a help to the nurse in training, as well as to the graduate, and has this advantage as a reference-book that it is not made cumbersome by unnecessary information. J. N. H.

INTERNATIONAL CLINICS. Edited by A. O. J. KELLY, A.M., M.D., Philadelphia, Pa., U. S. A. Vol. I., fourteenth series, 1904. Pp. 304. Philadelphia: J. B. Lippincott Company, 1904.

TREATMENT occupies the first place in this volume, and a prominent one, both from the value and variety of the subjects presented in it. This is especially gratifying to the practical physician who wishes more upon the "what to do" than upon the "what it is" and "how it came to be so," which to many workers seems to be sufficient. The Chloride Reduction Treatment of Parenchymatous Nephritis by Widal and Javas places this therapeutic suggestion upon a sound practical basis and suggests much in the way of betterment of long-continued and generally difficult conditions. In adonidin, a chemical study by Wilcox, a paper illustrated by sphygmographic tracings, shows clearly both the applications and limitations of this little-used remedy. Colloid silver, by Netter and Solomon, gives us the final word upon a much-discussed subject, and with it we are inclined, from our personal experience, to agree. Edes, a veteran in clear-headed logic from his vast experience, offers the question, "What is the cure for neurasthenia?" and answers it in his inimitable way. We will delay the passing of neurasthenia, as one of our neurologists would advise us, until the broad view of the author has taken root and yielded beneficent results. And, finally, McCaskey goes over the Treatment of Gastric Neurasthenia and Allied Conditions, and points out the way in which the physician should travel to keep these patients from hope-

less invalidism. Davis, upon the Treatment of Pneumonia, gives the commonplace facts, but with the added attraction of personal experience. We quite agree that alcohol has been administered with too free a hand, but its entire omission is decidedly difficult in those habituated to its use. Cattell presents an exceedingly readable paper on Cryoscopy, assembling its important literature and reaching thoroughly practical conclusions. With this in hand the average practitioner should have no difficulties. Favill gives one of his thorough expositions of nephritis of gastrointestinal origin. Walsh pleads for an early diagnosis of pulmonary tuberculosis, and gives information as to how it may be reached. Beck, on Angioma and its Treatment, gives an interesting summary, although his illustrations are open to criticism. Clark and Luther critically review Methods of Intestinal Anastomosis. Gaston writes an appreciative paper on the Complications Encountered in the Surgical Treatment of Diseases of the Testicle. An observant traveller, Noble, faithfully records his wandering in quest of surgical novelties, and records his findings in three of the best German clinics. The ingenious Griffith offers a new mallet for surgical use, which impresses us by its attractive theory. Non-operative gynecology, an unfashionable subject, if Davenport's paper receives proper attention, may bring within the purview of the specialist some facts which apparently have been neglected, while Craig believes that there is even a non-operative treatment of chronic ovarian lesions. Peripheral neuritis, by Pritchard, is singularly attractive, both in form and matter. The progress of medicine during the year just passed is presented by Edsall, Bloodgood, and Stevens. Here quality rather than quantity is noticeable, and the result is good, even if imperfect. This volume is more than fully illustrated, and the quality of plates far above the ordinary. To say that this is well up to the standard of its predecessors is but just to an excellent volume of the series. R. W. W.

LEHRBUCH DER GYNAKOLOGIE. By MAX RUNGE. Berlin: Julius Springer, 1903.

To anyone familiar with the first edition of Runge's work no comment is needful regarding this second edition, except to say that it has kept pace with the changes and modifications which our knowledge or the lack of it has in the last few years brought about in our conceptions of the truth of gynecology.

To those who do not know this valuable and most interesting book, we would say that it is in no sense a surgical manual, but that for the man engaged in general practice it is, in our opinion,

one of the best of volumes. It is true that some of the teaching is not in accord with that accepted in this country. This is notably the case in the directions for the repair of lacerations of the pelvic floor and the local treatment of the endometrium.

The chapter on the use of the pessary to correct retrodisplacements is admirable, but the section devoted to the consideration of operative interference in this condition is, in our opinion, poor, as he describes the operation of ventrofixation, but does not mention ventrosuspension. The methods advocated for the operative after-treatment cannot be commended in certain respects.

The chapter on fibroid tumors of the uterus is interesting: as might be expected, he is rather enthusiastic upon the vaginal method of attack. Judging from the experience of operators in America, his opinion as to the curability of cancer of the cervix would seem rather too enthusiastic. He insists, however, most strongly upon the necessity of the early diagnosis, and advocates the dissemination among the laity of scientific knowledge bearing on this point.

The section devoted to syncytioma malignum is very brief. We feel that this is a mistake. The section upon diseases of the ligaments of the uterus, pelvic connective tissue, and peritoneum is particularly well done.

The chapter upon Gonorrhœa is good, with the exception that the local treatment of the disease when limited to the genital tract below the cervix is not detailed as fully as the importance of the subject would warrant. As a whole, the book is, as we have said, a very satisfactory volume for the man who wishes a clear and concise view of gynecology from the non-operative standpoint.

W. R. N.

Blood Pressure in Surgery. An Experimental and Clinical Research. The Cartwright Prize Essay for 1903. By George W. Crile, A.M., M.D., Professor of Surgery, Western Reserve Medical College; Visiting Surgeon to St. Alexis Hospital; Associate Surgeon to Lakeside Hospital, Cleveland. Philadelphia and London: J. B. Lippincott Company, 1903.

The careful and extensive experimental investigations which are the subject of this treatise form a valuable and interesting addition to our knowledge of surgical shock and collapse, and will probably have much influence on the scientific treatment of these conditions. The experiments lead to conclusions which are somewhat at variance with the commonly accepted ideas of stimulation. In experimental shock few drugs were found to be of value in relieving the condition or in raising the blood pressure. It is interesting and surprising to learn that therapeutic doses of strychnine are inert and that physiological doses are dangerous or fatal. Cardiac stimulants have

but a limited range of usefulness in shock and may even be injurious, but in collapse they may be useful. In shock saline infusion raises but cannot sustain the blood pressure. Adrenalin was the only drug which was found to have a markedly beneficial effect. It raises the blood pressure in the normal animal, in every degree of shock; when the medulla is cocainized; and in the decapitated animal. Its effects are fleeting, and it should be given continuously. By means of adrenalin the circulation of a decapitated dog was maintained for ten and one-half hours. By the combined use of artificial respiration, rhythmic pressure upon the thorax, and the infusion of adrenalin, animals which were apparently dead as long as fifteen minutes were resuscitated. A pneumatic rubber suit, which produced an artificial peripheral resistance, was found to be of additional value in raising the blood pressure. By means of this apparatus, combined with the procedures just mentioned, a patient, who, from a fatal injury of his brain, had been conventionally dead for nine minutes, was partially resuscitated for thirty-two minutes, during which time a strong heart beat was noted, and he was able to move his head. W. T. L.

Chart of the Sympathetic Nerve (Life Size). By Byron Robinson, of Chicago. Chicago: E. H. Colegrove, 1904.

The operations upon the cervical sympathetic ganglion which have been recently frequently discussed have brought this portion of the nervous mechanism prominently before the surgical world, and it follows naturally, therefore, that the anatomy of this system should be carefully understood by the profession. Robinson's chart will be found of considerable aid in this study. J. H. G.

Modern Microscopy. A Handbook for Beginners and Students. Combining: I. Microscope and Instructions for its Use, by M. I. Cross. II. Microscopic Objects: How Prepared and Mounted, by Martin J. Cole, Lecturer in Histology at Cooke's School of Anatomy. Third edition, entirely revised and enlarged, to which is added: III. Microtomes: Their Choice and Use. Chicago: W. T. Keener & Co., 1903.

The book is not specially prepared for the physician or medical student and could be of little value to those working in the special branches of scientific medicine. There is no attempt to make the book one of reference, and most of the technical methods are given

in a very elementary form. Perhaps the best portion of the book is that devoted to the microscope. Part II., which deals with the preparation and mounting of microscopic objects, is not confined to a consideration of medical subjects. Animal tissues are considered, but there are also chapters upon the preparation of crystals, botanical mounts, and entymological specimens. The metric system is not used. Many of the methods are described too briefly to be clear.

Altogether the book does not seem to be well suited for use in the modern laboratory. W. T. L.

THE STRUCTURE OF THE GLANDS OF BRUNNER. By ROBERT RUSSELL BENSLEY. Printed from Volume X. of the Decennial Publications of the University of Chicago.

THIS monograph consists of a careful histological study of the glands of Brunner of one marsupial and of nineteen placental species, microchemical and staining methods being especially applied to the solution of the problem.

After a general review of the work done on this subject, which shows the various conclusions reached by different investigators, Bensley first describes the glands of Brunner in the opossum; descriptions of these glands of the cat, dog, mink, raccoon, hedgehog, ten genera of rodents, sheep, pig, and man follow.

The results of this investigation show that there is a remarkable uniformity in the nature and structure of the glands of Brunner of many mammals. In eighteen out of the nineteen genera examined the glands are of a pure mucous type. This conclusion is based on the structure of the cells of the glands and on their staining and microchemical properties.

The structure of the cells also supports the conclusion, Bensley thinks, that they are mucous cells. He considers that they are certainly primitively cells of the same type as the pyloric cells; he does not feel, however, that Oppel's theory, which holds that Brunner's glands are developed as a farther downward growth of the pyloric glands into the intestines, can be reconciled with the facts of their distribution and of their ontogenetic development. Bensley believes it to be more probable that they are cænogenetic structures developed in mammals from the hypoblast of the midgut. He does not consider the evidence that he has brought forward to show the glands of Brunner are mucous glands, to exclude the possibility of their also forming digestive ferments in quantities too small to be recognized by present methods.

The monograph covers 146 pages and is supplemented by an extensive bibliography and six plates. G. C. R.

Charles White, F.R.S., A Great Provincial Surgeon and Obstetrician of the Eighteenth Century. An Address Delivered Before the Medical Society of Manchester, October 7, 1903. By Charles J. Cullingworth, M.D., F.R.C.P. Lond. London: Henry J. Glaisher, 1904.

In the general interest which has been taken in the characters of the great medical teachers and surgeons and physicians of London and Edinburgh in the eighteenth century, many really great provincial medical men have been more or less overlooked, and their services to the advancement of the profession neglected. The present address serves to revive the memory of one whose very name is largely forgotten outside of the town of Manchester in which he practised. Dr. Cullingworth's address is accompanied by a number of valuable illustrations, and is a most interesting portrait of a bygone medical worthy. F. R. P.

Nervous and Mental Diseases. By Archibald Church, M.D. and Frederick Peterson, M.D. Fourth edition. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

The fourth edition of a book the size of the volume under consideration should not need extended reviewing. The existence of a fourth edition in such a short time is evidence that it fills a distinct want in its chosen field, and it will be necessary to consider only the changes from the previous edition.

The most important change is the addition of a chapter by Adolph Meyer reviewing the work of the German schools and their influence on the methods of study and teaching of psychiatry. This critical analysis of the development of psychiatric thought and methods covers 38 pages of very fine print. It is a masterly piece of work, and not only thoroughly reviews the subject, but also has the added value of a scientific analysis from one who thoroughly knows his subject and has devoted much thought and work to it. It will, no doubt, convince the reader and the investigator that what we need is "less discussion of generalities and more records of well-observed cases, and especially records of lifetimes, not mere snatches of picturesque symptoms or transcriptions of the meaning of traditional terms." There are many questions about our patients which the average work on insanity does not attempt to answer or even discuss; for those who have not the time or the ability to consult the "productive pioneers" in this field this digest offers the method for arriving at the solution of such questions.

The classification of the previous edition is retained. Although this classification was the subject of much criticism in the reviews

of the previous editions, there is little doubt that a clear-cut clinical description of the "established clinical entities" is of much more value to the student than a more complex classification based on more or less hypothetical and psychological ground. The success of this text-book has established this fact and has also shown that for the purposes of the student it is advisable to combine the study of psychiatry and neurology.

The sections on diseases of the nervous system have not been changed to any extent. New matter has been added on the following subjects: the healing of nerves, intermittent limping, herpes zoster and its relation to disease of the posterior roots, and the myoclonic form of epilepsy. The value of astereognosis and Kernig's sign in the diagnosis of nervous affections has received careful consideration.

The book is well printed on excellent paper, is well illustrated, and carefully indexed. D. J. M.

A TEXT-BOOK OF OPERATIVE SURGERY, COVERING THE SURGICAL ANATOMY AND OPERATIVE TECHNIC INVOLVED IN THE OPERATIONS OF GENERAL SURGERY. WRITTEN FOR STUDENTS AND PRACTITIONERS. By WARREN STONE BICKHAM, Phar. M., M.D., Assistant Instructor in Operative Surgery, College of Physicians and Surgeons, New York; late Visiting Surgeon to Charity Hospital, New Orleans, etc. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

THE object of the author of this work is to offer to the student and surgeon a reliable guide for the various operations of general surgery, and especially to call attention to the surgical anatomy and technic. The subject is presented in a clear and most systematic manner, and but few criticisms can be made of the work.

Parts of the book, such as the chapters dealing with the surgery of the heart and bloodvessels, deserve particular commendation. A careful consideration has been given to the latest operations, and the book may be considered up-to-date.

The illustrations are largely new and thoroughly serve their purpose.

The author has seen fit to exclude from consideration the operations of plastic surgery, which we think is a mistake, since one would naturally turn to such a work to find a description of the more common of these operations, such as harelip and cleft palate. We think this criticism is just, in view of the fact that the author includes the operations upon the female generative organs, which are to be found in every work on gynecology, whereas separate

volumes dealing with plastic surgery are not very numerous and are not possessed by a large proportion of the profession.

For operations upon the extremities we have seen few books which present a more reliable guide.

We are surprised to find that the pyloroplasty of Finney is not described among the operations upon the stomach. Another omission which we consider regrettable is that of Doyen's operation for the radical cure of hydrocele. The operation described for the cure of varicocele is the low operation, and not the high one which is so generally employed at the present time. In comparison with the space devoted to ligations and amputations we feel that the subject of the radical cure of hernia has been given too brief a consideration. A criticism which might be made of the author's style is that a systematic method of considering each operation necessitates considerable repetition, but the justness of this criticism might be questioned.

Looking upon the work as a whole, it can be said that it is one of the best and most reliable books of its kind. J. H. G.

DISEASES OF THE SKIN: AN OUTLINE OF THE PRINCIPLES AND PRACTICE OF DERMATOLOGY. By MALCOLM MORRIS, Consulting Surgeon to the Skin Department, St. Mary's Hospital, London; Corresponding Member of the K. K. Gesellschaft der Aertze in Wien, etc. With two colored plates and fifty plain figures. New edition. Chicago: W. T. Keener & Co., 1903.

THIS new edition of Mr. Morris' manual of *Diseases of the Skin*, which is apparently the third, contains a considerable amount of new material and a number of new illustrations. Sections descriptive of *blastomycetic dermatitis*, *porokeratosis*, *parakeratosis variegata*, and of the so-called *tuberculides* of the French authors are the most important of the new additions to the text.

We note that the author is ultraconservative, perhaps, concerning the use of the Finsen light, and more especially the *x*-ray, in the treatment of lupus vulgaris, the latter agent being dismissed in less than two lines. Tuberculin is still believed to be a useful remedy in this disease, an opinion which probably finds but few supporters at the present time.

The nature of Darier's "corps ronds" in keratosis follicularis (*psorospermose folliculaire vegetante*) is regarded as still an open question; but if we are not mistaken, Darier himself sometime ago gave up the idea that these bodies are parasitic.

Except in a few minor matters the present edition is well up to date, and the practitioner will find it, like previous ones, a clear and faithful presentation of dermatology as it is taught to-day.

M. B. H.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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The Diagnosis of Gastric Carcinoma.—JULIUS SIGEL (*Berl. klin. Wochenschr.*, 1904, xli. pp. 299, 338) has investigated in Ewald's clinic the value of the newer methods suggested as useful in the diagnosis of gastric carcinoma. The tryptophan reaction proposed by Erdman and Winternitz he found unsatisfactory. It was positive in only 2 out of 15 carcinoma cases; this corresponds with the previous report of Glässner, who found it positive in 1 out of 12 cases of carcinoma, in 2 out of 6 cases of ulcer, and in 1 case of gastric catarrh.

Although the method of determining the amount of albumin and urea in the washings of the fasting stomach, as proposed by Solomon, does not lead to absolute results, Sigel thinks it of some aid in diagnosis. While 4 cases of ulcer gave albumin and urea values much below the cases of carcinoma, a case of benign stenosis of the pylorus following an ulcer gave high values for both, and it is just in such cases of stenosis that a differential diagnosis is of the highest importance. The differences in cases of chronic gastritis and carcinoma are very marked in his table, and although he admits that a case of simple gastritis might rarely produce an excessive secretion of albumin, neither he nor Solomon have observed such a case. In the case of an obscure abdominal tumor with indefinite gastric findings he correctly ascribed the tumor to the stomach on the basis of high albumin and urea values in the washings. Gluzinski's[1] method to differentiate simple gastric ulcer from carcinoma developing in the base of an old ulcer by determining a relative insufficiency in the hydrochloric acid secretion likewise gives valuable but not absolute results. Out of 13 cases operated on or followed clinically, in 12 this method gave results corresponding

[1] The method of Gluzinski is to estimate the amount of free HCl in the stomach at three periods on the same day: 1. In the morning, fasting; the stomach is washed. 2. Three-quarters of an hour after a test breakfast of egg-albumen. 3. Four hours after a test meal (beefsteak).

with the correct diagnosis. In 1 case, however, in which the finding pointed to carcinoma the patient recovered completely. In 2 further cases in which there was a palpable tumor and all evidence pointed to the existence of a malignant growth, the Gluzinski method gave constant high free HCl values, and both proved to be benign.

In a third case, however, in which the free hydrochloric acid ran 17, 16, 22, the tumor was found at operation to be a carcinoma.

Sigel finds that the estimation of the fatty acids in the urine, a procedure advised by Rosenfeld, gives results too variable to be of any value in diagnosis.

Factors Influencing the Coagulation of the Blood in the Living Organism.—Boggs (*Deut. Arch. f. klin. Med.*, 1904, lxxix.), has investigated very thoroughly the influence of various substances in reducing the coagulation time of the blood. In his first experiments with gelatin he obtained a marked influence on six guinea-pigs, the coagulation time dropping rapidly from a normal of 6 minutes to as low as ½ to 1 min. in twelve to twenty-four hours, and rising again to the normal in the course of several days. This result is unique, and he was never able to obtain it again, although he varied the experiments in every conceivable manner and used various breeds of guinea-pigs. In all instances the influence was negative or so slight that it fell within the range of normal variation. He is inclined to explain the remarkable result to a racial peculiarity. With gum arabic the time was slightly reduced (from 5.5 and 5 min. to 3.5 min.), but the influence lasted only from 15 to 30 min. With cows' milk the result in two instances was a marked negative influence (from 4.2 and 6 to 12 and 11.5 min.) after a short and slight positive phase (4 min.). The serum of different animals injected into guinea-pigs gave various results. Serum from a goose produced marked reduction in the coagulation time (from 4.3 to 2 min.), while dogs' serum gave partly positive, partly negative phases, the two often following one another in rapid succession. Antileukocytic serum had no effect on the coagulation time in a dog. Extracts of various organs (thymus, liver) showed constantly a positive action. From a clinical standpoint the results with the calcium salts were the most interesting. In some of his investigations he substituted calcium lactate for the chloride, which has the same effect on the coagulation time, is tasteless, and is well borne. In his experiments on animals with calcium chloride a reduction in the coagulation time was never missed, the effect lasting on an average from two to three hours. In a guinea-pig, for instance, with a coagulation time of 5 min., 25 c.cm. of 1 per cent. soluble calcium chloride was introduced intravenously at 6.30 P.M. At 6.48 P.M. the coagulation time was 1.5 min.; at 7, 1.5 min.; at 7.10, 2.5 min.; at 7.35, 2.5 min.; at 10.30 A.M., 6 min. The calcium salts given to human beings by mouth produced a distinct reduction in the coagulation time, this result being absent in only a single instance. Examples: from 5 min. to 3.2 min., from 7.7 min. to 5 min., from 6.7 min. to 3.7 min., from 9.7 min. to 6 min. In one instance of purpura there was a reduction of from 21 minutes to 6.

[These observations quite support the experience in Professor Osler's wards, where the value of the calcium salts in increasing the coagulability of the blood, especially in cases of jaundice in which surgical interference is necessary, has been clearly proven.—W. S. T.]

A Contribution to the Study of Paroxysmal Hæmoglobinuria.—DONATH (*Zeit. f. klin. Med.*, 1904, Bd. lii., Heft 1 and 2) reports very fully three cases of paroxysmal hæmoglobinuria induced naturally and experimentally by exposure to cold, and reviews the various attempts that have been made to explain the origin of this condition. In numerous experiments made with suspensions of red blood cells drawn from the finger before, during, and after attacks, he was unable to demonstrate any abnormal susceptibility of the corpuscles to cold, agreeing with the observations of Ehrlich, Boas, Chvostek, and others. Contrary to the findings of Lichtheim and Chiaruttini, there was no solution of the hæmoglobin when the blood was coagulated at various temperatures. All these cases showed slightly diminished resistance of the red blood corpuscles to mechanical insults, but the results varied considerably in the same case at different times, and there was a marked individual difference between the several cases. The variation from normal was always small and altogether out of proportion to the ease with which exposure to cold precipitated an attack. There was no such susceptibility to mechanical influences as apparently existed in the cases of Chvostek and Chiaruttini. Hæmoglobinuria occurred in one case after simple ligature of the finger or arm. In the other two cases the procedure gave negative results. Luzzatto and Sargente have shown that this hæmoglobinuria following stasis is not due to mechanical injury, but to thermic influences, the solution of the hæmoglobin not occurring when the normal temperature of the ligatured extremity is maintained. Donath was unable to demonstrate any direct decrease of resistance in the red blood corpuscles to cold or mechanical influences. He attempted to produce evidence in support of Ehrlich's view that in these cases under the influence of cold the blood serum gained a red blood corpuscle dissolving property. The serum obtained during an attack and during the interval was tested in varying dilutions with the red blood cells of the same individual, of normal individuals, and of patients with other diseases. In several instances the serum showed a slight hæmolytic effect on the cells of other individuals, but the effect was the same with the interval serum and the attack serum, and in no way above the normal isolytic action exhibited by various sera. In only one instance did the attack serum show a hæmolytic effect slightly above the interval serum.

In none of the three cases did the interval serum show autolytic properties, and although this is opposed to results published by other authors, he concludes that the property must at least be variable and cannot be accepted as the rule. In one case the attack serum showed a slight autolytic property.

Donath points out that although he has been unable to demonstrate the presence of a hæmolysin in his cases, this is no argument against the existence of such a property; for if a toxin be formed there is opportunity enough for it to become immediately anchored, and it could be demonstrated only if present considerably in excess of the amount bound by the susceptible red blood corpuscles, *i. e.*, those with suitable receptors. Attempts to "activate" inactive interval serum by the addition of attack serum, supposing complement to be produced in excess during an attack, proved fruitless, as did also efforts to reactivate inactive attack serum by adding active interval serum or active normal serum on the supposition that amboceptors might be produced in excess.

In order to see if the red blood corpuscles themselves were more susceptible to hæmolytic influences, he subjected the cells from his cases to serum from other individuals, to hæmolytic immune serum and to certain red blood corpuscle dissolving substances, such as abrin and ricin. The results show that the red blood cells in his cases have the same relation to human serum from other sources and to hæmolytic immune serum as the erythrocytes of other cases, while abrin and ricin agglutinate them in somewhat weaker solutions. By collecting serum from the arm of different patients after having put on a compression ligature and immersed them in cold water for from six to ten minutes, he was able to show in two out of four cases a slightly increased hæmolytic action of such serum on the red blood corpuscles, not only of the hæmoglobinuria cases, but also of a number of other patients.

Donath thinks he is justified in concluding that the blood disintegration does not follow as a result of the direct action of cold or of purely mechanical influences upon the red blood corpuscles, but is due to hæmolytic properties of the serum. He believes this property to depend upon substances similar to the serum hæmolysins.

Pneumococcus Peritonitis.—Anton Ghon (*Wiener klin. Woch.*, 1904, xvii. p. 267) reports four cases of acute fibrinopurulent peritonitis due to diplococcus pneumoniæ. The first case was that of a girl, aged twenty-three years, who was taken suddenly ill with pain in the abdomen and died on the fourth day of general peritonitis. Autopsy showed a diffuse fibrinopurulent peritonitis and a perforated gastric ulcer. Cultures from the exudate gave a pure growth of pneumococcus. In Case II. there was a diffuse serofibrinopurulent peritonitis following perforation of a gastric carcinoma. Cover-slips from the exudate showed very numerous definitely lancet-shaped diplococci, retaining the Gram stain, and a small number of bacilli. The colonies on agar plates were chiefly of pneumococcus. Case III. was one of diffuse fibrinopurulent peritonitis developing eight days after gastroenterostomy for carcinomatous obstruction of the pylorus. Cover-slips from the exudate showed principally Gram-positive lancet-shaped diplococci and a few short bacilli. In cultures only a bacillus identified as colon grew, but inoculation of the exudate into a mouse produced death in twenty-four hours from pure pneumococcus septicæmia.

In Case IV. there was a deeply ulcerated gastric carcinoma without perforation, marked secondary hepatic and glandular involvement, fibrinopurulent peritonitis localized about the region of the pylorus, and fibrinopurulent meningitis. Cultures from the meninges and the swollen glands along the greater curvature gave a pure growth of pneumococcus. Cover-slips from the peritoneal exudate showed only lancet-shaped Gram-positive diplococci, but in cultures there were also a few colonies of colon bacillus and two colonies of staphylococcus aureus.

Although in three of these cases the pneumococcus was not found in pure culture, Ghon feels justified in assuming that it was the active agent. He quotes Jensen, who, in twenty cases of pneumococcus peritonitis, found three following perforation of gastric ulcer, and Brunner, who collected twenty-two cases of perforated gastric ulcer, examined bacteriologically and found four due to pneumococcus. Ghon considers the mouth and pharynx the source of infection. In Case III. there

was a lobular pneumonia from which a pure culture of pneumococcus was obtained, while clinically the pulmonary involvement preceded the symptoms of peritonitis.

SURGERY.

UNDER THE CHARGE OF

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The Surgical Treatment of Epilepsy.—J. CHALMERS DA COSTA (*Medicine*, February, 1904), in an admirable review of this subject, states that in determining upon the course of treatment for a person suffering with epilepsy due consideration should be given to the possibility of effecting cure by or of obtaining benefit from a surgical operation. An opinion to be of value must emanate from some one who possesses a scientific knowledge of epilepsy and has examined the patient with painstaking care; who has secured an accurate history of the sufferer's previous life, of his diseases and accidents, of his hereditary tendencies, and of the exact character of his convulsive seizures, and, finally, the decision should be made by one who has a surgical conscience. Operating without conscience is not only ruin of the soul; it is often the ruin of the patient, and it is always to the infinite disgrace of the medical profession. It is known that epilepsy is quite common, but exactly how common is somewhat uncertain. According to Spratling, in the United States one person out of every five hundred of population is epileptic, and in Europe the proportion is slightly less.

The surgeon must always bear in mind that many and quite different causes have been assigned for epilepsy, and that our conception of the pathology of the disease is not an established certainty, but rather a probability or a guess. The conclusions that one should draw from the views of modern students are that epilepsy is a diffuse lesion of the cortex of the brain, and that the conditions pointed out as causative may not infrequently be the result of the disease. Epilepsy is usually regarded as without danger to life, but Spratling points out that in this disease there is a distinct tendency to sudden death. Occasionally, though very rarely, patients recover from epilepsy without any treatment at all. If cases are treated early and carefully, and are placed under proper control, from 8 to 10 per cent. may be cured, but if the attacks have lasted over two years or have been very violent there is almost no hope of effecting a cure by medicine. Thus it may be seen that we are dealing with a distressing and usually incurable disease,

which, as a rule, unfits the patient for duties of active life, and which, as a general thing, gradually drags him into the ruin of dementia. In such a dreadful condition there is every justification for the performance of operation, if operation even offers a chance. All sorts of methods of treating this disease have been adopted in the past, and every few weeks a new method is suggested. There is scarcely a drug in the *Pharmacopœia*, there is hardly a material in the vegetable world or in the mineral kingdom that has not been at some time or other employed and lauded. Although modern medical treatment has been somewhat more successful than the ancient plans, epilepsy is still with us to a fearful extent.

In setting forth the surgical treatment of epilepsy the author states that he will not discuss the various peripheral operations that may be performed with the idea of eliminating a focus of irritation or of intercepting some irritant impulse. That such operations are occasionally beneficial is undoubted. The author has seen great improvement or apparent cure follow the removal of a tender cicatrix and follow the performance of circumcision in a case of phimosis. Nevertheless, the curative influence of such operations is occasional rather than common, and it is the purpose of this article to dwell particularly upon operations upon the skull and brain. The confidence in the curative value of brain operations in epilepsy has very much diminished in recent years; in the author's opinion less than 5 per cent. are cured by this means. Previous observers have been deceived by the fact that any operative traumatism may for a time improve, and even greatly improve the manifestations of the epileptic condition. This phase of the question was most ably presented some years ago by Dr. J. William White in his well-known article upon the curative effects of the operation *per se*. A case should not be reported as cured until at least three years have elapsed since the operation was performed, and five years is probably a safer limit. Operation in any case should only be resorted to after a most careful study of the patient, and preferably a neurologist should be associated with the surgeon in making this examination. Then, too, the patient should be under observation for some days by either a physician or a nurse, so that the convulsion and sequelæ may be accurately noted in writing, and this report should prove of great help in reaching a conclusion. From a surgical standpoint epilepsy should be classified into different forms, in some of which operative interference is distinctly contraindicated, for the reason that it not only does not do any good, but in some cases may make the patient distinctly worse. 1. Idiopathic epilepsy: Uncomplicated cases of essential epilepsy should not be operated upon, because operation will never bring about a cure. However, if an epileptic suffers with persistent localized headache, it is justifiable to trephine, to open the dura, and to inspect the brain. Even if no cause for the headache be discovered the patient may often be relieved or cured of the pain. In such a case an osteoplastic resection should not be performed, and the trephine button should not be replaced. In status epilepticus the cerebral pressure is notably increased, and trephining with drainage of the ventricle is justifiable to relieve pressure that might cause death. Operation in ordinary essential epilepsy for the relief of the increased intracerebral pressure, as recommended by Kocher, has the objection that there is the danger not only of infection but also of hernia cerebri, and,

as Clark has pointed out, this excessive intracerebral pressure is a result rather than a cause of epilepsy. Jaboulay's operation of the excision of the cervical ganglia of the sympathetic for the relief of essential epilepsy has not been followed by very brilliant results. Winter has collected 122 cases, in one-half of which there was no apparent improvement. 2. Idiopathic epilepsy with focal symptoms: Many of these cases, which begin within the first two years of life, are due to unrecognized cerebral infantile palsy. If, from the very start, the convulsive attacks have had a local beginning, and if the surgeon has seen the case within two years of the first attack, it is proper to trephine and excise the irritated portion of the cortex. This is true whether the convulsions remain partial or spread to the rest of the body, and whether consciousness is lost or not. Operations in children are more hopeful than in adults. After the condition has persisted for two years, however, operation offers practically no hope of cure, as the association fibres are by that time hopelessly degenerated. In performing this operation it is impossible to avoid removing more of the cortex than merely the excited centres of the motor region. After the operation there is, of necessity, paralysis of the parts controlled by the extirpated centres. This paralysis is usually first temporary, though the finer movements are never regained. The earlier the operation is done the better is the prognosis. In these cases an osteoplastic operation should be performed. In those cases of genuine essential epilepsy in which after a time the convulsions have taken on a focal character operation offers no hope of curing the disease, although even in these cases operation may become necessary if the great frequency of the attacks produces exhaustion and threatens life. Again, it is possible that in a case of essential epilepsy a gross cortical lesion may develop and may lead to the production of Jacksonian seizures. In such a case one might be driven to operate for the gross lesion, without having any hope of curing the generalized epilepsy. 3. Traumatic epilepsy: When epilepsy ensues upon traumatism the attacks frequently do not begin until some months or a year or more have elapsed; in fact, several years may elapse between the time of the injury and that of the development of epilepsy. An injury may be followed by generalized epilepsy or by Jacksonian epilepsy. The more time that has elapsed between the reception of the injury and the performance of the operation the worse is the prognosis. Traumatic Jacksonian epilepsy gives a better prognosis from operation than does any other form of the disease; where there is a distinct neurotic history the prognosis is worse than when such a history is absent. The prognosis is much better in the Jacksonian than in the generalized form. Every operation in traumatic epilepsy is exploratory. Any obvious lesion should be extirpated, but if nothing be found on exploration, and if the attacks have been distinctly focal in origin, it is justifiable to extirpate the motor centre from which the discharge seems to originate. When the injury is in the motor region the chances of cure are much better than when the sensory region is involved, but when the frontal region has been the seat of injury operation offers very little hope of cure. 4. Jacksonian epilepsy due to gross brain disease: This condition demands the treatment of the underlying brain disease. 5. Epilepsy following infantile cerebral palsy: In the cases associated with congenital cerebral palsy operation in childhood is justifiable, but not promising; but when the patient

has reached adolescence operation is useless. 6. The posthemiplegic epilepsy of adults: In these cases operation is entirely valueless.

The conclusions deducible from the preceding remarks are as follows: 1. Operations for epilepsy are distinctly disappointing and rarely curative, and are indicated in only a small proportion of cases. 2. They frequently produce temporary benefit. 3. They may save life, but they are not entirely free from danger, and occasionally leave the patient worse than before. 4. The mortality, though small, is not inconsiderable. 5. The actual number of complete recoveries is probably under 5 per cent. 6. No case should be claimed to have been cured until from three to five years have elapsed since the operation. 7. Even after operation medical treatment and supervision should be exercised for a long period of time.

THERAPEUTICS.

UNDER THE CHARGE OF

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Adrenalin in Ocular Therapeutics.—M. Darier, at a meeting of the Société d'Ophthalmologie de Paris, spoke as follows of the use of this drug in ophthalmology: As a means of diagnosis of beginning iritis it is very useful when there is hesitancy in instilling atropine. By means of it episcleritis may be easily differentiated from pustule of the limbus. Certain doubtful forms of conjunctivitis may be recognized as granular by its use. From a therapeutic point of view, adrenalin exaggerates the action upon the eye of the various alkaloids; cocaine anæsthetizes an inflamed eye without otherwise affecting the organ if adrenalin has been first applied. Combined with it, cocaine will render great service in conjunctivitis and lessens the pain of topical applications as well. Its use makes catheterization of the tear-duct unnecessary, for a simple injection does away with the stenotic action of the mucous membrane. When eserine or atropine fail in their usual action upon the pupil, combination with adrenalin obviates the difficulty. Its use facilitates operations upon the conjunctiva because of the ischæmia which it produces, but after iridectomy its employment may be followed by hemorrhage into the anterior chamber. In corneal lesions, such as ulcerations, it should not be used, but in episcleritis it produces excellent results.—*Revue de thérapeutique*, 1904, No. 9, p. 313.

Adrenalin in Glaucoma.—Dr. Grandclément reports an instance of severe and marked glaucoma cured by this agent. The treatment consisted in the instillation into the affected eye every half hour for three consecutive days of a 1:5000 solution of adrenalin. The course and outcome of this case encourage the belief that it may be possible to cure the various forms of glaucoma by this simple means,

doing away with the difficult and painful operation of iridectomy. The chief element in the treatment is to know how to employ this strong and dangerous vasoconstrictor. Two points must be carefully noticed: (1) To instil the adrenalin sufficiently long to momentarily stop the secretion of the intraocular fluids and to cause a perceptible diminution of the tension. (2) To carefully avoid the production of a dangerous and irremediable hypertension.—*Journal de médecine de Paris*, 1904, No. 17, p. 167

Adrenalin in Cancers of the Respiratory Passages.—M. MAHER has employed this agent in cancers of the larynx and of the mouth with the result of improving the condition of the patients, suppressing the tendency to hemorrhage and lessening the pain. M. ICHARD has in a number of cases obtained an almost complete cicatrization of the ulcerating surfaces and has stayed the growth of the lesions in one patient for a period of sixteen months. A 1 : 1000 solution was at first employed, but it had the disadvantage of deteriorating rapidly upon exposure to the air. A permanent powder, such as the following: adrenalin, 5 parts; tartaric acid, 5 parts; sodium chloride, 90 parts, from which a fresh solution of 1 : 1000 strength may be readily made, obviates this difficulty. The applications of the adrenalin are usually made every two days. By this treatment epitheliomata of the larynx, of the tongue and of other regions, such as the breast, are greatly relieved.—*Journal de médecine et de chirurgie pratiques*, 1904, No. 7, p. 258

Iodine Glycerole in Granular Conjunctivitis.—DR. JABLOWSKI has obtained excellent results from the employment of this remedy in this condition. The strength of his solution is 1 part in 60. With this he paints the inflamed conjunctiva. The application is only slightly painful, and the treatment seems to have a particularly favorable action upon old granulations which have become acutely inflamed and in recurrent cases which have been treated with silver nitrate. Also in trachomatous pannus the iodine acts well and is likely to cause permanent cure. The duration of the treatment varies with the gravity of the lesion. Cure is usually complete after from three to four months of daily applications.—*La semaine médicale*, 1904, No. 15, p. 120.

Intravenous Injections of Sodium Salicylate in Rheumatism.—DR. FELIX MENDEL reports excellent results from this treatment, even in rebellious cases. His formula is as follows, the caffeine being added to lessen the tendency to local irritation: sodium salicylate, 2.2 drachms; caffeine, 20 grains; distilled water, 12.5 drachms. Thirty minims of this solution are injected and repeated twice a day in severe cases. In those less severe the injections may be given as infrequently as every three days. In 80 cases of monarticular and polyarticular rheumatism, sciatica, lumbago, and rheumatic pleurisy so treated the effects have been very good. The injections are given into one of the larger veins of the arm.—*La semaine médicale*, 1904, No. 16, p. 128.

Quinic Acid in Gouty Conditions—DR. J. WEISS advocates the use, in these conditions, of quinic acid alone, or, perhaps, preferably, in combination with lithium, the combination being termed urosin. In

dosage of from 3 to 4 drachms daily it diminishes the excretion of uric acid appreciably and increases the output of hippuric acid to a considerable extent. In arthritic conditions with pain, stiffness and tophi, the administration of from 45 to 75 grains daily, best taken dissolved in water after meals, in divided doses, affords marked relief. The author considers that in urosin we have a remedy for the uric-acid diathesis as efficacious as is quinine against malaria or salicylic acid against acute rheumatism.—*Wiener klinische therapeutische Wochenschrift*, 1904, No. 18, p. 493.

Sodium Sulphanilate in Exophthalmic Goitre.—Dr. Kirnberger bases his theory of this treatment upon the idea that the condition is an autointoxication due to the superproduction of iodothyrin by the hypertrophied thyroid gland. Knowing the efficacy, as exploited by Ehrlich, of sulphanilic acid and its sodium salt in the treatment of iodism, the author has used these means in exophthalmic goitre. The dosage was at least 2.5 drachms per day, which was well tolerated and productive of good results. In all cases the drug had a calming effect, increased the patient's strength, and diminished the tachycardia. In most cases the tremors and the size of the thyroid were uninfluenced. The author concludes that the drug is merely palliative in its effects and to be employed to relieve the symptoms, either alone or in connection with other treatment.—*Revue francaise de médecine et de chirugie*, 1904, No. 16, p. 381.

The Treatment of Cardiac Insomnia.—Dr. Feilchenfeld states that insomnia at the commencement of cardiac insufficiency manifests itself thus: After a deep slumber of two hours or so the patient will awake with obstinate oppression and palpitation; further sleep is often impossible, and the same phenomena reappear night after night. Upon examination of the heart nothing is found, and the insomnia is attributed to nervousness. Such sleeplessness should be treated at first by hygienic measures and hydrotherapy; later, if necessary, hypnotics (morphine, sulphonal, codeine) may be prescribed, but only in small doses. Large doses do not cause sleep, but aggravate the patient's condition. The author has achieved good results from 0.25 grain of powdered digitalis, combined with 0.125 grain of morphine hydrochlorate, given during the evening, and 0.125 grain of sulphonal given several times during the afternoon. Large doses must be avoided, and it is remarkable what good results are obtainable.—*Berliner klinische Wochenschrift*, 1904, No. 11, p. 282.

The Medical Treatment of Pyloric Stenosis.—M. Thaon states that the first consideration in the treatment of this affection is regulation of the diet. Strict milk diet, three or four quarts in twenty-four hours, should be prescribed, together with wet compresses over the epigastrium. When there is severe pain bismuth, in doses of from 3 to 4 drachms, mixed with 6 ounces of water, should be given. Following this treatment a gradual return to solid diet is allowed. Sodium bicarbonate is useful to correct hyperacidity, and in fermentative conditions, antiseptics, such as ammonium fluoride, iodized sulphur, benzonaphtol, betol with bismuth salicylate, resorcin with bismuth, or spraying with silver nitrate solution, may be employed. When there is pyloric spasm,

large doses of oil are recommended, and a properly fitting girdle, together with massage, may prove efficacious. When the stasis is considerable we may have recourse to hypodermic injections of about 12 drachms of serum, followed by gastric lavage, with 0.9 per cent. salt solution. In cases with moderate stenosis simple lavage may be employed and followed by lavage with powdered meat; otherwise the diet should be exclusively of milk. In tetanic conditions lavage is also useful.—*Revue francaise de médecine et de chirurgie*, 1904, No. 18, p. 424

Isopral, a New Hypnotic.—Dr. Impens reports this substance is trichloro-isopropylic alcohol and possesses the following properties: It crystallizes in white crystals fusible at 49° C., but subliming at ordinary temperatures. It is soluble in alcohol, ether, and water, but in the last less so than chloral, to which substance isopral is comparable. It has a camphor-like odor and an aromatic and slightly irritating taste. Upon contact with alkalies and heat it loses its chlorine without the formation of chloroform. Physiologically the action of isopral is twice as intense as that of chloral, without an equal possibility of poisoning.—*Journal de médecine de Paris*, 1904, No. 16, p. 157.

Intratracheal Injections of Eucalyptol in Pulmonary Tuberculosis and Chronic Laryngitis.—M. Atony concludes, as the result of experiments, that the treatment of certain forms of chronic laryngitis and of most types of pulmonary tuberculosis by intratracheal injections of oil of eucalyptol has these advantages. It is easy of application, well borne by the patient, and brings about good results. By it the digestion is not disturbed, and it is less painful than the various hypodermic treatments. The patients do not object to it, it does not interfere with their work, and the technique of its application is simple. The author uses a mixture of 5 parts eucalyptol to 95 of olive oil at first, but gradually increases its strength until an 8 per cent. mixture is reached. The first injection consists of 15 minims, and if well borne the quantity is increased up to 45 minims, and the treatment is given daily or upon alternate days. Of 15 cases of tuberculosis, 3 were benefited, and in 2 cases of laryngitis regularly treated the results were most favorable.—*Archives de médecine et de pharmacie militaires*, 1904, No. 5, p. 381.

Beer Yeast in Exanthemata and Erysipelas.—MM. Presta and Tarruella have treated a number of patients with scarlatina and measles with beer yeast with rather remarkable results. Most of the observations were taken during epidemics in which there were numerous fatal cases and cases complicated with meningitis, bronchopneumonia, nephritis, etc., but the patients treated with the yeast, for the most part, became convalescent within three or four days after the appearance of the exanthem, and in no case so treated did the disease last longer than sixteen days. The yeast seems to cause a marked diminution in the desquamation of scarlet fever, and under its influence the eruption of measles quickly disappears. After a few doses the scarlatinal angina disappears, as also does the albuminuria, if it be present. Twenty-four cases of erysipelas were markedly influenced by the administration of the yeast; the high temperature and other symptoms quickly disappeared. In four days the local lesions became merely slight redness and infiltration, and these manifestations disap-

peared by the sixth day, followed by desquamation. The constitutional symptoms ameliorated within forty hours and disappeared in about three days. In advanced cases with complications, such as anuria, cardiac insufficiency, hyperpyrexia, and pulmonary congestion, the treatment produced good results, and there was no recurrence of the malady, even though some of the cases had suffered previous attacks. In all cases the dosage was from 4 to 6 coffeespoonfuls of the dry yeast every twenty-four hours.—*Revue francaise de médecine et de chirurgie*, 1904, No. 15, p. 354.

PEDIATRICS.

UNDER THE CHARGE OF

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The Association of Chorea with Tænia Solium.—JAMES BURNET, of Edinburgh (*British Journal of Children's Diseases*, April, 1904, p. 147), reports two interesting cases under this title. The first case was that of a girl, aged seventeen years, but looking very much younger. Her illness was of five days' duration, the movements beginning upon the right side, but rapidly becoming generalized. She had had a slight choreic seizure four years before. It was impossible to obtain a history of rheumatism, although there was a strong family tendency to that disease, the mother being rheumatic and a sister having developed chorea following an attack of acute rheumatism. The patient's movements became so violent that at times she had contrived to throw herself out of bed upon the floor. There was no murmur, but the heart seemed to be dilated.

Under the ordinary treatment with salicylate of sodium there was no improvement until, the possibility of tapeworm being considered, a dose of male fern was administered, and a large tænia solium, without the head, was expelled. From this time she continued to improve, and after the expulsion of a large number of segments with the head, following another dose of the anthelmintic, she made a prompt and complete recovery.

The second case was that of a girl, aged twelve years, who, a year before the onset of her chorea, had had an attack of pleurisy, with pains in both lower limbs. She had never been quite well since that attack, having become pale and nervous.

There was no cardiac murmur, but the second pulmonary sound was accentuated. She was given antirheumatic treatment, with arsenic in addition. Her condition after several weeks became serious, with a temperature of 101°, rapid pulse, and embarrassed respiration. Having in mind his previous case, which resisted routine treatment, the author

resolved to try the effect of an anthelmintic upon this patient. Accordingly, a dose of extr. filicis liq. was administered, which resulted in the expulsion of a complete tænia solium of fair size. There was a rapid disappearance of the symptoms almost immediately. The author believes that chorea, even in rheumatic subjects, may have its origin in causes other than the rheumatic toxin, and that the possible presence of tapeworm should always be borne in mind in those cases which are not amenable to the usual routine treatment.

Enuresis in Children.—Percy Lewis (*British Journal of Children's Diseases*, February, 1904) gives a plan of treatment for this troublesome condition, which he has successfully carried out in his practice.

His observations show that most of the subjects of this complaint are children unhealthy in aspect, of irregular habit in regard to their diet, and living mostly upon farinaceous and saccharine foods; that they are difficult to arouse from sleep, and even if taken up at night quickly relapse into a kind of stupor upon being returned to bed. He has also noted that these children pass larger quantities of urine in a single night, which is of low specific gravity, of neutral or alkaline reaction, and with a deposit of triple phosphates or oxalates. He infers from the way in which the bed is "deluged" that the bladder is not emptied until it is full, and that on account of the unirritating urine the "call" to the central nervous system is sufficient only to start the necessary reflex for emptying the bladder, but not enough to awaken the patient.

This condition, he considers, is analogous to the polyuria of infants fed upon starchy foods, whose symptoms rapidly disappear under a proper change of diet. So in the older children, with both polyuria and enuresis, a marked improvement is noticed after the introduction of a rigid antidiabetic diet. As most of the cases are much depressed in health, a general tonic treatment is recommended at the same time. Without any other treatment he has observed rapid improvement, and finally cure in many cases, both in private and in hospital practice.

Influence of the Ingestion of Chloride of Sodium upon the Weight of Nurslings.—P. Nobecourt and G. Vitry (*Revue mensuelle des maladies de l'enfance*, March, 1904, p. 120) have investigated the influence of chloride of sodium upon the weight of nurslings in fourteen cases in addition to the series of eight cases reported by them last year (*Bull. de la Soc. de Pédiatrie*, December, 1903). The amount of salt given was 0.25, 0.5, and 1 gram per day, which was administered in one or two doses in a little boiled water before a nursing. Comparison of the babies' weight-change for periods of seven days with and without the addition of salt to the diet showed in general that increase in weight was greater during the weeks when they took salt than in the weeks without it. By comparing the increase in weight per 1000 gm. of body-weight, before and after the use of salt in the diet, they obtained a series of 42 observations, in some of which the same infant figured several times. In this series there were 27 favorable results and 15 unfavorable, though the latter all showed gains very little inferior to those of the period when salt was not taken. The ages of the infants varied from twelve days to four months, but the

good results were obtained without reference to the age at which the experiment was made.

The results seemed to be particularly successful with babies weighing less than 2 kgr., 500, for among 28 records 20 were favorable (71 per cent.), while the total percentage of favorable results was 64. It therefore seems that with premature and poorly nourished infants the addition of salt is especially valuable—an observation which appears to accord with the results of Nobecourt and Lemaire (*Bull. de la Soc. de Pédiatrie,* April, 1902), who found that the quantity of sodium chloride in kgr. of body-weight excreted by premature infants was greater than with other infants.

As to the effects of the different doses prescribed, all gave favorable results, but the smallest dose (0.25 gm.) gave 70 per cent. of successes, while 0.5 gm. gave 65 per cent., and 1 gm. only 58 per cent. These results are more striking if compared with the body-weight. In one class 1 cgm. of salt was given for 100 gms. and above to 140 gms., while in the second class 1 cgm. for less than 100 gm. of body-weight. In the first class there was 77 per cent. of successful results in all the cases, and 100 per cent. for infants below 2 kgr., 500, while in the second class there was only 63 per cent., and with doses of 1 cgm. for less than 50 gm. of weight it was 60 per cent. The larger doses sometimes gave rise to vomiting or diarrhœa.

The explanation of this improvement under the addition of salt is difficult. Various theories have been advanced: improvement of digestion and stimulation of general nutrition; increase of hydrochloric acid in the gastric juice; facilitation of the absorption of albumin. The authors suggest that it may be due to retention of water in the tissues because of insufficient renal elimination. Experimental investigation of the total urinary output of very young infants for several days, however, is practically impossible. Several observations of the blood in these cases, under the same conditions as to time, have shown no changes to indicate retention of water in the blood.

They therefore conclude that additional salt is valuable in the dietary of infants weighing less than 2 kgr., 500, and of premature infants, and that an average dose of 0.25 gm. per day, or, more exactly, 1 cgm. per 100 gm. of body-weight, is sufficient to give good results.

An Early Case of Friedreich's Ataxia.—At the February meeting of the Society for the Study of Diseases in Children (*British Journal of Children's Diseases,* May, 1904, p. 104) Mr. Jackson Clarke showed a case of Friedreich's ataxia in a boy aged four years. He had dropping of both feet, exaggerated knee-jerks, Babinski's sign, and the parents had noticed some weakness of the left hand. An older brother, in whom the symptoms had begun at six years, had rigidity of the lower limbs and wasting of the muscles of the thumb. In the line of treatment in the early stages light instrumental guidance was advocated; later, tendon elongation and tenotomy, followed by massage.

Herpes Zoster Associated with Generalized Bullous Eruption from Prolonged Administration of Arsenic—James H. Sequeira (*British Journal of Children's Diseases,* April, 1904, p. 158) records a case of herpes zoster caused by prolonged administration of arsenic, which

is interesting from the unusual association of a generalized bullous eruption. The patient was a girl, aged five years, who had been brought to the London Hospital in the summer of 1902 suffering from psoriasis. Three minims of Fowler's solution three times a day were ordered, and the lesions treated locally with an ointment of ichthyol and salicylic acid. The patient lived in the country, and was seen only at long intervals, but the treatment was not intermitted. About three months after the treatment was commenced the mother stated that she noticed that the skin of the trunk was darker than normal, but she attributed the change in color to the ointment. About four months after the child was first seen, during which time she was known to have been taking arsenic (though it is possible that the drug had been administered some time before) she was brought to the hospital with a crop of vesicles and bullæ all over the trunk. The lesions varied in size from that of a pin's head to 5 mm. in diameter. They were round, tense, and contained a clear fluid, and there was a narrow zone of hyperæmia around each. On the loin, hip, and the upper part of the thigh and the anterior aspect of the lower part of the abdomen of the right side there was a copious eruption of herpes zoster, corresponding with Heid's first lumbar area. The skin of the trunk was also pigmented. The color was a pale, yellowish brown, with the peculiar dappled appearance of arsenical pigmentation. The psoriasis had almost disappeared. The face and extremities were entirely free from vesicles, and the pigmentation was limited to the parts covered by the clothing. The child was in perfect health, and at no time had presented any signs of acute arsenical poisoning.

The arsenic was stopped, and all the lesions rapidly dried up, but the pigmentation persisted, beginning to disappear only after a year. The scars of the herpetic lesions persisted, but there was no scarring in the site of the bullæ.

A Contribution to the Study of Cerebrospinal Meningitis.—M. B. Auche (*Revue mensuelle des maladies de l'enfance*, January, 1904, p. 20) reports a case of pneumococcic cerebrospinal meningitis, which is noteworthy from the fact that its evolution was slow and that recovery ensued.

Diplopneumococcic meningitis is notably of greater gravity than the more frequently encountered meningococcic variety. In general, its onset is sudden, its evolution tumultuous, and its course rapidly fatal, especially in the metapneumonic cases. Rarely are cases observed in which the evolution is slow and the termination favorable.

The patient was a boy, aged five years, who had previously been in good health. He had coughed for several days before coming under observation, and had slight headache, an evening temperature of 103°, with frequent vomiting of a greenish, bilious fluid. At the base of the left lung was a small area of fine subcrepitant rales, without signs of consolidation. These symptoms rapidly subsided, and the temperature began to fall, but then appeared the first symptoms of meningitis, which, however, developed quite slowly. The symptoms noted from time to time were intense headache, without the hydroencephalic cry; repeated vomiting at the beginning; moderate constipation; pupillary dilatation equal on the two sides; photophobia; rigidity of the neck and trunk; Kernig's sign; slight exaggeration of the tendon reflexes;

rapidity and sometimes a little irregularity of the pulse; retraction of the belly—the tâche méningitique. There were no delirium, agitation, convulsion, or paralysis. The temperature was irregular, oscillating considerably within short periods. These symptoms lasted about five weeks, when they began to subside, and convalescence ensued. Three lumbar punctures were made, from the first two of which cultures showed colonies of a diplococcus exhibiting the biological and morphological characteristics of the pneumococcus. Its virulence was slight, since it failed to kill rabbits, and after the second puncture scarcely affected them.

This observation is of especial interest, since it illustrates the fact that with lessened virulence the pneumococcus may produce meningitic symptoms, which, from their slow onset and protracted course, resemble those of the milder cases due to the meningococcus.

OBSTETRICS.

UNDER THE CHARGE OF

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Eclampsia, its Causation and Treatment.—In the *Archiv für Gynäkologie*, Band lxxii., 1904, ZWEIFEL gives the results of his studies in eclampsia and its treatment in the laboratories and wards of the Leipzig Clinic.

He reviews the literature of the subject, drawing attention to the theories of Frerich, Traube-Rosenstein, Munk, Bidder and Otto, Speigelberg, Halbertsma, Bouchard, Massin, Hahn, Volhard and Schumacher, Scanzoni, Stumpf, Schmorl, Butte, Dienst, Schröder, Zangemeister, and others.

From these and other investigations it seems proven that the cause of eclampsia is a poison formed within the body of the patient and circulating within her blood. This poison attacks the epithelia of the parenchymatous organs, damages the heart muscle, and extensively disorganizes the blood. It was the aim of Zweifel's studies to ascertain the nature and identity of this poison.

He first examined the urine of the patient with reference to the percentage of urea, in view of the fact that in man urea represents 83 per cent. of the nitrogenous excreta. He also investigated the quantity of ammonia, of uric acid, and of albumin. He also investigated the amount of nitrogen in the purin bases and studied the relation of these various substances in healthy patients, and in those suffering from eclampsia. He observed that in eclampsia the quantity of urea in proportion to the entire nitrogenous waste is greatly lessened and also that the greater the quantity of albumin the lesser the quantity of urea.

If the quantity of urea during eclampsia increased, the quantity of albumin grew less. He believed it to be shown that a careful estimate of the quantity of albumin during the progress of a given case would indicate the increase or lessening of the urea, and so the improvement or lack of improvement in the patient. Inefficient oxidation of albuminoid materials affords the most rational explanation for the condition of the urine seen in eclampsia. He also investigated the quantity of urea in the blood, and found that it was impossible to use this as a means for prognosis.

In estimating the salts of ammonium he reviews Zangemeister's results, who found increased excretion of compounds of ammonium in eclampsia. From his own investigations he concludes that the poison of eclampsia is an organic acid capable of oxygenation and readily changeable into various compounds. He draws attention to leucomaines and ptomaines, and also to the sulphates in the urine of eclamptic patients as indicating the degree in which the unknown acid remains free or undergoes combination. He finds that the severer the case of eclampsia the smaller the quantity of sulphates in the urine, and so the greater the quantity of neutral sulphur. This account points to lack of oxidation of albuminoid materials as the primary cause of eclampsia.

In searching further to determine the nature of this acid he finds that lactic acid is the only one demonstrated by his investigations which is poisonous and which is not formed in the metabolism of healthy human beings. It is significant that cases of nephritis without eclampsia do not give the same results when metabolism is studied.

Clinically, he calls attention to cases of epilepsy in which the convulsions occur and which may be mistaken for eclampsia. He draws attention to cases of poisoning in which patients die with convulsions which are not the usual eclampsia. He also remarks the tendency to eclampsia seen in multiple pregnancy, and the failure of the theory of dilatation of the ureters to account for eclampsia.

Clinically, it is of great interest to observe that eclampsia differs much in frequency and in mortality in various portions of the world. In Würtemberg and in Vienna eclampsia is much less common than in other portions of the Continent of Europe. The explanation for this is found in the use of light wines and beverages containing tartrates of sodium and potassium, which combine with bases in the food preventing the formation of lactic acid.

In the matter of treatment in prophylaxis Zweifel would limit strictly the quantity of meat and eggs eaten and encourage the use of fruits and vegetables. Sugar and starch do these patients no harm, and may be permitted. He would also give effervescing beverages containing the tartrates and carbonates of sodium and potassium freely.

In the actual treatment of the convulsion he calls attention to the danger of using narcotics and especially chloroform for an indefinite period, as fatty degeneration of the heart muscle and epithelia of secreting organs has been observed in these cases. He is not in favor of profuse sweating, although he faithfully tried it, but saw no benefit. Pilocarpine should, in his belief, never be employed.

Formerly Zweifel was in favor of waiting for spontaneous dilatation of the uterus before delivering the child. The mortality among his cases was 32.6 per cent. Immediate delivery was then practised by

Dührssen's method of incision for three years, when the mortality sank to 15 per cent., and in some series 11.25 per cent. Glöckner had a similar experience. Bumm divides his treatment of eclampsia into three periods: one in which narcotics were freely used with 30 per cent. mortality; a second period, when, in addition to narcotics, baths and packs were used, with 30 per cent. mortality; and a third period, when delivery as soon as possible after the first convulsion was practised, with a mortality of 12 per cent. In Ohlshausen's clinic convulsions ceased after delivery in 81 per cent. of the cases. A mortality of 16.9 per cent. occurred.

He believes that the general practitioner in the presence of eclamptic convulsions should immediately rupture the membranes, and that this will have a good influence in lessening the convulsions. When the cervix is partly dilated dilatation may be completed by the hand or elastic bags, and delivery accomplished by forceps or version. If the vaginal portion of the cervix is still present Zweifel believes that Dührssen's incisions or vaginal Cæsarean section by Dührssen's method or Cæsarean section by abdominal operation, as recommended by Halbertsma, should be practised. He does not incline to the use of Bossi's dilator.

The Scar of Uterine Rupture Found in a Uterus Removed by Operation.—In the *Monatsschrift für Geburtshülfe und Gynäkologie*, Band xix., Heft 6, 1904, Amann reports the case of a patient who suffered with a large abdominal hernia. During a difficult labor about two years previously, the patient had rupture of the uterus followed by the escape of the fœtus into the abdominal cavity. The physician in attendance performed abdominal section and sutured the uterus. Primary union did not occur, but suppuration persisted for some time with the formation of an extensive abdominal scar and hernia. The patient's condition was such as to greatly interfere with her work.

On examination a convolution of intestine as large as a child's head and covered by very thin integument was found protruding through the hernial opening. An abdominal cystic tumor was also present, which extended deeply into the pelvis.

On abdominal section the convolution of intestine was so adherent to the integument that its separation was performed with the greatest difficulty. The cystic tumor was intraligamentary and adherent to the intestine. The tumor was finally entirely removed, and was found to contain pus. The uterus was removed, the edges of the wound trimmed and brought together, and a drain of iodoform gauze passed through the abdominal wall and into the vagina. The hernial sac was dissected out, and the abdomen brought firmly together. The patient recovered without complications.

On examining the tumor it was found to be a suppurating dermoid. The tear in the uterus had extended from the lower uterine segment up upon the left side, and had opened into the left broad ligament. When the uterus was closed only the external tissues were brought together, and the muscular tissues remained ununited. As a consequence, the cavity of the uterus communicated with the cavity in the broad ligament. The dermoid tumor must have been a hindrance to labor, and may have predisposed to the rupture of the uterus. The suppuration of the dermoid tumor followed the primary operation

upon the womb. The adhesions were the natural consequence of the primary infection. The incomplete union in the uterine wall found in this case illustrates the rupture of the uterus after some of the primary and early operations for Cæsarean section. Those who performed these operations did not bring together the uterine wall accurately, but simply closed the peritoneal covering. As a result of this rupture readily occurred.

GYNECOLOGY.

UNDER THE CHARGE OF

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Vaginal Hysterectomy for Prolapsus.—STELZNER (abstract of Inaugural in *Zentralblatt für Gynäkologie*, No. 6, 1904) reports 80 cases from the clinic at Basle and Halle, with one death from causes foreign to the operation. Fifty-eight patients were kept under observation, 30 being entirely cured, 10 partially, while only 3 were unable to work. The ages of the patients ranged from thirty to sixty years.

Precocious Menstruation.—KLEMM (*Zentralblatt für Gynäkologie*, No. 6, 1904) reports the case of a girl, aged eleven years, in perfect health, who menstruated regularly every twenty-eight days. Although a child in other respects, her breasts and external genitals were fully developed, but not the sexual impulses. The writer collected 53 similar cases from the literature.

Treatment of Rupture of the Uterus.—SCHAEFFER (*Zentralblatt für Gynäkologie*, No. 7, 1904) reports 18 cases occurring in the Strasburg clinic in the course of ten years, 13 complete and 5 incomplete; 60 per cent. of the latter and 30 per cent. of the former recovered. Laparotomy was performed eight times, with four recoveries.

Anatomy of Chronic Metritis.—LORENTZ (*Archiv für Gynäkologie*, Band lxx., Heft 2) after his studies of nine uteri removed on account of persistent hemorrhage, agrees with Theilhaber's conclusions that the menorrhagia in chronic metritis is due not to disease of the vessel walls, but of the muscular tissue, which, being replaced by connective tissue, is unable to contract as usual. Hence venous stasis and hypertrophy of the uterus. Contrary to the usual opinion, the writer found no changes in the endometrium, and states that the commonly observed thickening of the vessel walls and consequent narrowing or closure of the lumen is not due to atheromatous changes, but is to be regarded as a physiological process the result of obliterating endarteritis.

THEILHABER (*ibid.*) in a paper on the same subject, based on examinations of one hundred uteri, emphasizes the fact that the essential pathological change in chronic metritis is connective-tissue hyperplasia of the myometrium rather than hyperplasia of the endometrium. Among etiological factors he enumerates adnexal disease, frequent childbearing, infection, parametritis, and sexual excess. Menorrhagia and leucorrhœa are the prominent symptoms. Curettement relieves the symptoms, but does not cure the disease.

Gonorrhœal Endometritis.—PARADI (*Orvosi Hetilap; Zentralblatt für Gynäkologie,* No. 7, 1904) has treated several hundred cases with intrauterine injections of argentamin (10 per cent.) and sodium lygosin (5 per cent.), with good results.

Primary Cancer of the Tube.—DIRNER and FONYO (*Szülészet és Nogyogyaszat; Zentralblatt für Gynäkologie,* No. 7, 1904) report two cases. The first was in a multipara, aged fifty years, who had had an abdominal tumor since the menopause, two years before. She succumbed to laparotomy from sepsis three days after double ovariotomy. Examination of the specimen showed primary adenocarcinoma of both tubes. Metastatic deposits were found in the diaphragm on autopsy. In the second case an ovarian cyst and enlarged tube were removed from a multipara, aged fifty-six years, who remained in good health three years after operation. Primary cancer of the tube was present.

Treatment of Retroversion.—GRAEFE (*Zentralblatt für Gynäkologie,* No. 7, 1904) believes that no treatment is necessary when the uterus is normal, since the symptoms are not due to the displacement alone, but to the accompanying neurasthenia. When the patient has a fixed idea that her trouble is due to the retroversion, he prefers Alexander's operation to the use of a pessary, especially if she is sterile.

The writer does not replace every retroverted pregnant uterus if the patient can be kept under constant observation, even though it may seem to be incarcerated (!). If the displaced pregnant organ is adherent he advises laparotomy. If it is hypertrophied or sensitive a pessary should be used; if the ovaries are also prolapsed operation is indicated.

SPERLING (*ibid.*) thinks that there are no symptoms characteristic of retroflexion, but that these vary according to the nervous condition of the patient. Hence in some women the displacement gives rise to no trouble. [These conservative views are timely when so many gynecologists are disposed to regard every case of displacement from a surgical standpoint.—H. C. C.]

Gonorrhœa of Skene's Glands.—POLLAK (*Zentralblatt für Gynäkologie,* 1903, No. 9) in a careful study of this subject, based on 100 cases of gonorrhœal urethritis, found gonococci in 45 per cent. In 68.8 per cent. of these one duct, and in 31 per cent. both ducts were involved. He describes at length an interesting case in which a husband was infected with gonorrhœa a year after the wife's initial infection, and, several months after repeated examinations of the urethral mucus had failed to show the presence of gonococci. Cocci were subsequently found in the ducts, in which they had evidently been present all the time.

Rectal Alimentation.—DEUCHER (*Korrespondenzblatt für Schweizer Aerzte*, Band xxxiii., Jahrg. No. 2) believes that the simplest solutions are best, preferably saline and sugar with opium. Concentrated solutions (10 to 20 per cent.) may be used without causing irritation if a little opium is added. He rejects milk, since the fat is not absorbed; milk-sugar is the form most likely to decompose in the intestines, and albumin and casein coagulate in the presence of colon bacilli. Milk added to other nutritive fluids favors this decomposition and hinders absorption. Alcohol should not be used per rectum if the stomach is irritable, since it increases the gastric secretions.

Method of Shortening the Round Ligament.—VILLARD (*Lyon méd.; Zentralblatt für Gynäkologie*, No. 7, 1904) makes a crescentic incision through the skin above the pubes, joining the external rings, pulls out the round ligaments and ties them over the recti muscles. Six successful cases are reported, three of the patients subsequently bearing children.

Treatment of Postoperative Intestinal Paralysis.—ARNDT (*Zentralblatt für Gynäkologie*, 1904, No. 9) reports a series of cases in which he used eserin hypodermically, never administering over 2 milligrams (gr. $\frac{1}{30}$) in the course of twenty-four hours. In all the cases there was marked tympanites, with pain, vomiting and rapid pulse, which symptoms were not relieved by gastric lavage and enemata. The patients (five) responded promptly to the treatment, flatus passing within two or three hours after the initial dose of gr. $\frac{1}{60}$.

Combined Cancer and Tuberculosis of the Uterus.—WALLART (*Zeitschrift für Geb. u. Gyn.*, Band l., Heft 2 and 3) adds a third case to the two reported by Kaufmann. In the first case the diagnosis was made by the presence of both cancerous and tubercular tissue in the material removed with the curette. The second patient developed cancer of the cervix subsequent to the secondary tubercular disease of the uterus.

In the case reported by the writer, the patient, aged thirty-seven years, had a circumscribed tubercular nodule of the corporeal endometrium associated with extensive adenocarcinoma. He infers that the combination is probably more common than is generally supposed, and that the presence of tuberculosis of the uterus may predispose the patient to the development of cancer.

The Curability of Cancer.—LOMER (*Zeitschrift für Geb. u. Gyn.*, Band l., Heft 2 and 3) collected from various sources records of 213 cases of uterine cancer treated with the cautery which were free from recurrence two years after operation; 149 patients were well after an interval of five years. Most of the patients had been regarded as inoperable. The writer believes that the effect of the heat is not only to destroy the cancerous tissue, but to effect such a radical change in the blood as to prevent recurrence. He insists on the application of the cautery to every suspicious nodule which appears in the scar after a radical operation, as well as on the necessity of repeated and thorough cauterization in inoperable cases. Arsenic should be administered as a routine measure.

Ureteral Surgery.—FRANZ (*Zeitschrift für Geb. u. Gyn.*, Band l., Heft 2 and 3) reports six cases of injury to the ureters during the course of difficult abdominal operations, in all of which the ureter was successfully implanted in the bladder.

The writer states, as the result of experiments and clinical observations, that the flow of urine through the implanted ureter is at first impeded in consequence of a localized œdema of the ureteral mucosa. This soon subsides, as a rule, though rarely complete occlusion of the duct may result. A certain amount of dilatation of both the ureter and the renal pelvis may follow this temporary œdema.

Advantages of Abdominovaginal Drainage.—OBERLAENDER (*Zeitschrift für Geb. u. Gyn.*, Band l., Heft 2 and 3) states that combined abdominal and vaginal drainage was employed in 20 per cent. of Orthmann's private abdominal sections between April, 1899, and April, 1902. Only two patients died.

The writer believes that this method is best for drainage, especially when a quantity of pus has escaped, when large raw surfaces are left, and when there is fear of a subsequent intestinal fistula.

Hæmatoma of the Ovary.—POTIER (*Revue de gynécologie*, vol. vii., No. 5) includes under this head only hemorrhages into Graafian follicle. He reports the case of a young married woman, where the diagnosis of ectopic pregnancy had been made. An ovary the size of a hen's egg was removed, which contained several hemorrhagic cysts communicating with one another, as well as a number of follicles containing blood. The cortex was thickened as the result of inflammation, so that the follicles could not rupture. The hemorrhage was supposed to be due to excessive coitus.

Pneumococcus Peritonitis.—v. BRUNN (*Beiträge zür klin. Chirurgie*, Band xxxix., Heft 1) reports 2 cases from the Tübingen clinic, making 72 now on record. The writer calls attention to the fact that the fluid in the peritoneal cavity is usually thick and fibrinous and that it tends to become encapsulated, thus rendering the prognosis favorable. These collections of fluid are most often found in the neighborhood of the umbilicus and in the iliac fossæ. The abdominal viscera are seldom involved, but the lungs, pleura, meninges and pericardium are frequently affected.

The disease is most common in girls under fifteen years, beginning as a pneumonia, followed by increased temperature, abdominal pain, vomiting and diarrhœa. The process is soon localized in the abdomen, and persists for several weeks, with variable temperature, moderate pain and gradual loss of strength. The fluid may be evacuated spontaneously, but surgical intervention is preferable. In adults the diagnosis is more difficult, as it is liable to be mistaken for typhoid or tubercular peritonitis. It is characterized by an acute onset, followed by localization in the abdomen. Early incision and drainage are indicated.

Sarcomatous Degeneration of Fibroids.—HAUBER (Munich inaugural dissertation: abstract in *Zentralblatt für Gynäkologie*, 1904, No. 11) found 3 cases among 138 cases of fibromyoma in Klein's clinic. He infers that about 3 per cent. of all fibroids undergo sarcomatous degen-

eration. After the menopause such tumors should never be regarded as harmless, but should be kept under constant observation, and should be promptly removed if they begin to increase in size. The statistics of myoma operations are now so good that it is better to extirpate them early rather than to wait until rapid growth is noted. An exception is made, however, in the case of tumors which increase in size under the influence of pregnancy.

DERMATOLOGY.

UNDER THE CHARGE OF

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A Papuloexudative Dermatosis Produced by Pilocarpine.—HALLOPEAU and VIELLARD (*Annales de Dermatologie et de Syphiligraphie*, 1904, No. 3) report a case of extensive eruption following the prolonged use of pilocarpine. The patient, a man aged fifty-two years, consulted a distinguished ophthalmologist for some trouble of vision, who diagnosed an episcleritis and increased ocular tension, for which he prescribed instillations of 0.05 per cent. solution of pilocarpine and hypodermic injections of 0.05 centigram to 1 centigram of the same drug. Under this treatment the vision improved, but after thirty-five hypodermic injections and about eighty instillations an eruption appeared which occupied the face, the trunk, and the limbs. This eruption was a polymorphous one, consisting of papules, vesicles, pustules, and impetiginous crusts; some of the lesions were umbilicated like the eruption of smallpox. Symptoms of systemic intoxication accompanied the eruption, and at the end of two months the patient died.

Histological examination of the eruptive lesions revealed an inflammatory exudate about the excretory ducts of the sweat glands. The authors conclude, from a study of this unusual case, that pilocarpine introduced into the organism for a prolonged period by hypodermic injection and by instillation may give rise to an eruption of umbilicated papulæ which are situated in the sweat glands, the place of election for the eruption being the face and limbs. The exudate, at first serous, soon becomes purulent. This eruption differs in its clinical characters from all the dermatoses hitherto described, and is accompanied by grave disturbance of the general health, particularly of cerebral and cardiac innervation. The eruption is unaccompanied by fever. No antidote for pilocarpine is known, nor any efficacious way of eliminating it.

The Cutaneous Manifestations of Appendicitis.—MOTY, in a communication made to the Société Francaise de Dermatologie et de Syphiligraphie (*Annales de Dermatologie et de Syphiligraphie*, 1904,

No. 2), calls attention to certain cutaneous troubles associated with appendicitis. These vary according to the form of appendicitis which produces them, being acute and transitory in the acute form of the affection, disappearing with the febrile period, but having a very long duration, with an insidious beginning in the chronic variety. The most frequent cutaneous manifestation of acute appendicitis is congestive redness of the right cheek, recalling that which is observed in pneumonia; this redness is rarely wanting in the febrile forms with sharp reaction. In graver cases labial herpes occurs, situated most frequently upon the right side, although it may also occur upon the left. The extent of the eruption is in proportion to the sharpness of the reaction; a group of herpetic vesicles covering a small part of the surface of the lip will ordinarily correspond to an acute appendicitis of moderate gravity, while a series of herpetic plaques extending toward the right ear will coincide with a more serious attack.

Cutaneous manifestations are much rarer in chronic appendicitis, the author having met with but a single case. A surgeon, after an attack of diarrhœa, the nature of which was misunderstood at the time, suffered from unilateral sweating of the head and neck, which persisted for ten years, with mild exacerbations when the patient's general health was not good or when he suffered from abdominal troubles. Immediately after an operation made necessary by a brusque attack of appendicitis the sweating disappeared.

Lupus Erythematosus with Bullous Beginning.—Audry (*Annales de Dermatologie et de Syphiligraphie*, 1904, No. 2) reports a case of erythematous lupus which followed an eruption of bullæ. A girl, aged thirteen years, who had at various times suffered from epileptiform crises, which were believed to be due to hysteria rather than to epilepsy, after taking bromide of potassium suddenly presented an eruption of bullæ covering the face. This eruption, after treatment with poultices, disappeared very slowly. Two years later, when Audry saw her for the first time, the face was entirely well, except two plaques in the malar region, which presented the features of a well-characterized erythematous lupus. Later the patient again had an eruption of small bullæ situated upon the lips and chin, which occurred independently of the administration of bromide of potassium, and disappeared in the course of eight or ten days without leaving any trace.

A Case of Larva Migrans.—Lenglet and Delaunay (*Annales de Dermatologie et de Syphiligraphie*, 1904, No. 2) report in detail a new case of this very curious affection. A joiner, aged thirty-nine years, having a furuncle upon the calf, treated it with a remedy of his own for ten days, viz., the application of live snails; later it was cauterized with the thermocautery. About a month later there was a dark-red plaque, the size of the palm of the hand, upon the outer side of the right calf, having in its centre the scar of the initial furuncle and the furrows of the thermocautery. Upon this plaque were a number of tunnels like enormous itch burrows, with red borders and whitish centres, distended by a seropurulent fluid collected here and there in drops. They were markedly elevated and measured at their greatest width 3 mm. These burrows ran in all directions, but there seemed to be one principal

burrow always running in the same general direction, of which the others seemed to be branches. They advanced at the rate of 3 cm. to 4 cm. a day. All efforts to find the parasite were in vain. Sections made of these burrows showed that they were situated within the epidermis, and in places some of the cells looked as if they had undergone disintegration and digestion. In the corium beneath there was a considerable infiltrate of lymphoid cells, among which, and in the cells included in the burrow, were a number of eosinophiles. The authors suppose that the parasite gained access to the skin through the poultice of snails applied to the furuncle by the patient.

Paget's Disease.—FABRY and TRAUTMANN (*Archiv für Dermatologie und Syphilis*, Band lxix., Heft 1 and 2) report the results of their study of a new case of this disease. They found nothing especially new as to the histology of the disease, but in the epithelium about the margin of the diseased area, in sections made from various portions of the eroded surface and the axillary gland of the affected side, they found, by staining with alum hæmatoxylin, peculiar round corpuscles with darkly stained margins and clear centres, which they regarded as yeast bodies. In sections these bodies formed coarsely granular masses contained in cavities in the cutis. Pure cultures were obtained within twenty-four hours. The authors conclude that Paget's disease is an affection *sui generis*, belonging neither to eczema nor carcinoma, which, owing to its very chronic course and situation in the epidermis, offers specially favorable conditions for the development of carcinoma. Should the presence of the yeast fungus be confirmed by subsequent investigations, the question would arise whether this malady should not be looked upon as a blastomycosis.

Tuberculosis of the Skin.—KLINGMÜLLER (*Archiv für Dermatologie und Syphilis*, Band lxix., Heft 1 and 2) reports some of the results of his study, clinical and experimental, of a number of tuberculous affections of the skin. In 18 cases of lichen scrofulosorum 3 followed injections of tuberculin; these 3 cases presented no appreciable clinical differences from the other cases. In not a single one of the whole series of cases was it possible to demonstrate the presence of the tubercle bacillus, although more than 700 preparations were examined. The form which followed tuberculin infections was observed only in those who already showed evidences of tuberculosis or scrofula, although many such injections were made in other patients for the purpose of learning whether, beside some dermatosis, tuberculosis or scrofula existed.

As eczema scrofulosorum, the author reports the case of a young woman, who, besides lupus vulgaris of the forearm and a lichen scrofulosorum, had a brownish-red, scaly patch upon the calf, which was not well-defined, but gradually faded away into the surrounding parts. Examination of an excised portion of the patch showed a slight perivascular infiltration about the horizontal and ascending branches of the papillary vessels and a tubercle-like focus with giant and epithelioid cells in the fat tissue. No tubercle bacilli were demonstrable. The author thinks it possible that this patch may have been a beginning erythema induratum.

A case of lupus vulgaris occurring at the site of a tuberculin injection

also was observed in a woman who had suffered from lupus of the upper lip and the nose. The histological changes present in this lesion were like those seen in ordinary lupus tissue.

As to the etiology of lichen scrofulosorum, Klingmüller believes it is an affection which occurs only in tuberculous subjects, not as the direct effect of the tubercle bacillus, but through toxic materials produced by this organism. Lupus vulgaris is caused by virulent tubercle bacilli capable of multiplication. As the skin and subcutaneous tissue do not offer favorable conditions for their multiplication, they are found in small numbers. The author thinks the case of inoculation lupus reported makes the supposition probable that the extensive tissue changes in lupus arise from the action of toxic matter coming from the bacilli, which may be either an excretion product of the living organism or an extract of dead bacilli.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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The Elastic Tissue of the Ventricles of the Heart.—Poscharisky (*Ziegler's Beiträge*, 1904, Band xxxv. p. 510) studied the elastic tissue of the ventricles in a number of animals and in fifty individuals dead of various diseases. Of these fifty hearts only one was normal. Sections through the ventricle of this normal heart showed that the adventitia about the large bloodvessels was richly provided with elastic fibres, which ran from this zone along the coarser bundles of connective tissue that pierce the ventricular wall as well as into the heart's flesh, where they surrounded the muscle cells in the form of loops. From the epicardium as well as from the endocardium elastic fibres spread along the vessels into the myocardium. In 70 per cent. of the hearts from persons over forty years of age an increase could be made out in the intermuscular elastic fibres. In persons under this age it was rare to find such an increase. The striking hyperplasia of the elastic tissue seen in chronic myocardial affections appeared either in the adventitia of the vessels or in the outer layer of the endocardium, but the intermuscular fibrils played no part in the process.

Improved Technique of Agglutination Test in Typhoid Fever; the Use of Formalized Cultures.—It has been shown by Pröscher that a twenty-four-hour bouillon culture of bacillus typhosus which has been killed with formalin gives the same specific agglutinating reaction as the living culture when mixed with blood or blood serum from a typhoid-fever patient.

REUDIGER (*Journal of Infectious Diseases*, 1904, vol. i. p. 236) describes a method of using this reaction for clinical purposes. A large quantity of plain bouillon (100 to 1000 c.c.) is inoculated with bacillus typhosus and incubated at 36° C. for twenty-four hours. Afterward 1 c.c of formalin is added for every 100 c.c of bouillon. The culture is now ready for use, except that it must be shaken before it is used, because the dead organisms gradually settle to the bottom. A culture prepared in this manner can be kept for many months. To perform the serum test four drops of the patient's blood are collected in a small test-tube containing 2 c.c. of a 1:500 solution of formalin in distilled water. By this means the blood becomes laked, and a clear solution of the blood in approximately a 1:10 dilution is obtained. To 1 c.c. of the blood solution 4 c.c. of the dead cultures are added, making a dilution of about 1:50. The tube is now set aside. A control tube is made by mixing 1 c.c. of a 1:10 solution of normal blood or 1 c.c. of distilled water with 4 c.c. of the culture. If agglutination takes place the dead organisms collect in clumps, and within an hour or two are seen as a flocculent precipitate settling toward the bottom, leaving the bouillon clear at the end of twelve to twenty-four hours. In a series of experiments the agglutinative reaction obtained with dead and living bacilli were compared, and it was found that the two methods gave practically the same results. This method of performing the serum test with dead bacilli obviates the necessity of living cultures, microscope, and other apparatus outside of a few small test-tubes, and seems to the author suitable for hospitals, boards of health, and private practice.

The Chemistry of the Urine in Diseases of the Pancreas.—It is now admitted by most authorities that in fat necrosis consecutive to certain diseases of the pancreas, the masses of free fatty acids or the combination of them with lime, which constitutes the lesion, are directly derived from the fat of the affected part by the fermentation of the pancreatic secretion, and that the other constituent of the fat molecule, viz., glycerin, is absorbed in the circulation. Catillon has shown that if glycerin is given by mouth to dogs 50 to 60 per cent. of the amount is excreted in the urine. With this idea in mind CAMMIDGE (*Lancet*, 1904, i. p. 782) has studied the urine in cases of pancreatic disease, and finds that by certain methods it is possible to demonstrate a constituent which is not present in normal urines. This substance is glycerin. By heating the urine with nitric acid the glycerin is converted into glycerose. For the detection of glycerose phenylhydrazin was employed. To carry out this test two procedures are necessary:

(*a*) The urine is filtered and 10 c.c. are poured into a small flask; 1 c.c. of strong hydrochloric acid is added, and, a funnel having been placed in the neck to act as a condenser, the flask is placed on a sand-bath and gently boiled for ten minutes after the first sign of ebullition has appeared. A mixture of 5 c.c. of the filtered urine and 5 c.c. of distilled water is then poured into the flask, which is afterward cooled in running water. The excess of acid is now neutralized by slowly adding four grams of lead carbonate, and after standing for a few minutes to allow of the completion of the reaction, the urine is filtered through a moistened filter paper, and the flask is washed out with 5 c.c. of distilled water onto the filter. To the clear filtrate are now added 2 grams of powdered sodium acetate and 0.75 gram of phenylhydrazin hydro-

chlorate, and the mixture is boiled for from three to four minutes on a sand-bath. The hot fluid is then poured into a test-tube and allowed to cool undisturbed. After the lapse of from one to twenty-four hours a more or less abundant flocculent yellow deposit is found at the bottom of the tube, which consists of sheaves and rosettes of golden yellow crystals. As both sugar and albumin vitiate the experiment these substances must be thoroughly removed before the test is made. Since it was found that the urine not only in pancreatitis but in carcinoma of the pancreas and in certain other conditions when there was a destruction of tissue yield these crystals, a second experiment was necessary to eliminate these factors.

(*b*) 20 c.c. of urine are filtered and thoroughly mixed with half its bulk of a saturated solution of perchloride of mercury. After standing for a few minutes, it is carefully filtered, and to 10 c.c. of the filtrate 1 c.c. of strong hydrochloric acid is added. After this procedure the steps are the same as in (*a*). If the case is one of pancreatitis the yellow crystals are not found in the urine treated by the (*b*) process. In malignant disease the crystals are present. Besides this differentiation the crystals showed varying degrees of solubility in strong sulphuric acid. Crystals from cases of acute pancreatitis dissolve in from a few seconds to half a minute. Crystals from cases of chronic pancreatitis dissolve in one to two minutes, while in carcinoma of the pancreas solution takes place in from three to five minutes.

Observations made with the urine from three cases of acute pancreatitis, fifty-one cases of chronic pancreatitis, and fifteen cases of malignant disease showed that the test was surprisingly accurate. Mistakes are more likely to be made in cases of cancer of the pancreas, although in thirteen out of the fifteen instances a correct diagnosis was made by the urine examination. The author considers the reaction of great assistance in differentiating the acute and chronic forms of pancreatitis from diseases simulating these conditions.

Change in the Spleen in Pernicious Anæmia, etc.—Kurpjuweit (*Deutsch. Archiv für klin. Med.*, 1904, Band lxxx. p. 168) studied, by means of smear preparations and sections, the cellular elements of the spleen from cases of pernicious anæmia and from other diseases. He finds in every spleen finely granular cells which he interprets as myelocytes. Eosinophilic myelocytes and normoblasts are only seen in spleens which have suffered alteration through congestion, infectious processes, and severe anæmias. The author believes that under certain conditions the spleen may undergo myeloid transformation, partly through the proliferation of the pre-existing myelocytes and partly through emigration fo other cells, to which class belong the eosinophiles and normoblasts.

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SEPTEMBER, 1904.

APHASIA AND THE CEREBRAL ZONE OF SPEECH.[1]

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The cerebral zone of speech includes an extensive cortical region, probably not less than one-third of the cortical expanse of the lateral aspect of the left hemicerebrum, as shown in the shaded portion of Fig. 1. While for descriptive purposes it is best to designate it as a cortical area, it must be understood that both the cortex and subcortex of the entire region enter into its formation.

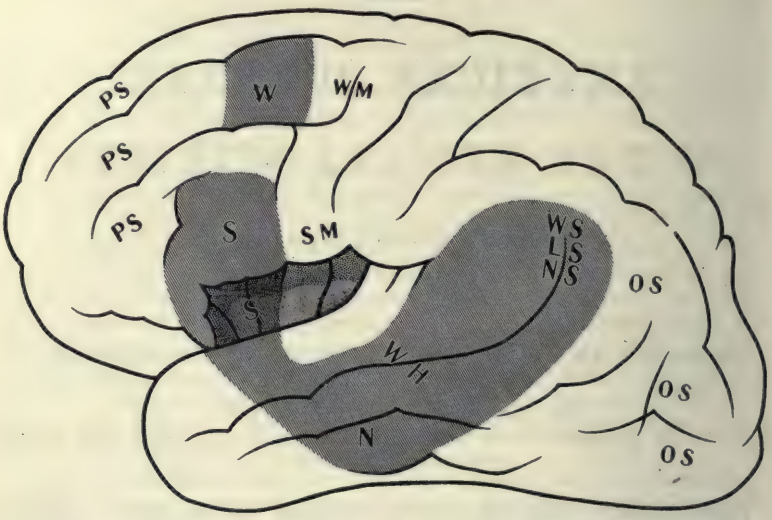
Within this great zone are several important centres or subareas concerned with particular attributes of language. In Fig. 1 these centres are *A*, a centre for word-hearing, the auditory portion of the zone of language; at *B* and *b*, a great centre for speech, often called the motor centres; at *V*, a visual subarea concerned with the representation of words, letters, and numbers; at *G*, a graphic or writing centre, usually spoken of as the motor graphic centre; and at *N*, a naming centre in which it is believed by those who hold to its existence that names are correlated with the concrete concepts of the objects named. In the diagram Fig. 2, in which the most important of the fundamental physiological areas of the cerebrum are represented graphically, these centres in the zone of language are more definitely isolated and designated by the terms word-hearing, speech, word-seeing, letter-seeing, number-seeing, writing, and naming.

Briefly stated, the auditive centre for speech is situated at the junction of the first and second temporal gyres about opposite the point where the horizontal branch of the Sylvian fissure turns upward posteriorly; the dynamic or motor speech centre occupies

[1] A paper presented to the College of Physicians of Philadelphia, June 1, 1904.

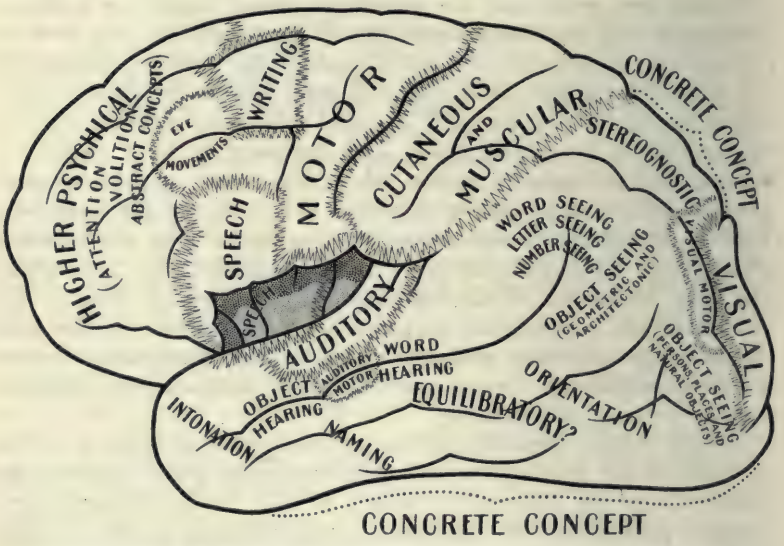
the hinder portion of the subfrontal or third frontal convolution, and, according to the views of the writer, the insula or at least its

FIG. 1.



Cerebral zone of language: *W*, writing centre; *S*, *S*, speech centre (language arrangement for emission); *WH*, word-hearing or auditory centre; *WS*, word-seeing; *LS*, letter-seeing; *NS*, number-seeing; *N*, naming centre; *PS*, *PS*, *PS*, higher psychic region; *WM*, centre for movements of upper extremity concerned in writing; *SM*, centre for movements concerned in speaking; *OS*, *OS*, *OS*, area for object-seeing.

FIG. 2.



Diagrammatic scheme of the physiological areas and centres of the lateral aspect of the human hemicerebrum.

anterior half; the visual centres immediately concerned with speech are located in the angular gyre; the site of the graphic or writing centre is in the caudal half or third of the second frontal convolution, and the naming centre is probably situated in the third temporal convolution.

Connecting these centres with each other, and also with other portions of the brain, are subcortical tracts composed of the processes of the cell bodies which are located in the cortex and of their fibrillary constituents. These associating tracts are of a complicated kind, although their number and arrangement are capable of analysis if sufficient time and study are given to the matter. Only one or two points regarding them need here be emphasized, namely, that the different centres are connected each to the other by a system of to-and-fro association, so that the impulses from special areas probably pass in both directions.

Surrounding the zone of language on all sides are centres and areas which have important relations to the function of speech. These are of at least three kinds, and an understanding of them may be reached by a study both of Fig. 1 and Fig. 2. On the sensory or receptive side of the brain are areas or centres concerned with such functions as object-seeing and object-hearing. Objects which are not recognized cannot of course be named, and these centres for object-recognition, therefore, are necessarily contributors to the sensori concept side of the zone of language. They are represented in Fig. 1 at the points marked as *OS*, and in Fig. 2 by the designation object-seeing, with subareas for geometric and architectonic forms, and for persons, places and natural objects. On the motor or emissive side of the cerebral speech zone are centres at *SM* and *WM* which are concerned with the execution of the work prepared for them respectively by the speech and writing centres. They are, in other words, the centres of representation of movements of articulation and enunciation, and of the movements of the hand and upper extremity generally. At *PS* in the prefrontal portion of the brain is a region where the highest psychical functions are especially represented. It is evident that in using language, attention, volition, and reasoning play a part, although this part may vary within wide limits. This higher psychical region, therefore, has its particular relation to the zone of language and especially to its dynamic side.

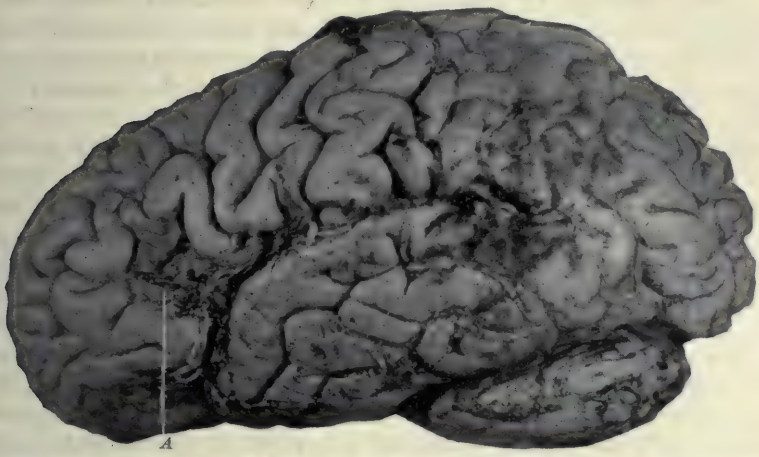
Broad, and it may be somewhat loose, comparisons may be helpful to the understanding of an intricate subject. The zone of language and that from which it is derived and with which it is correlated may be compared to the machinery and the methods by which one of our great natural products, like oil, is handled. The centres for object-recognition and the primary percept centres through which their memorial images are obtained may be compared to the producers or feeders of the system, the zone of language

with all its centres and their connections to the refiners of the raw product, the executive motor centres and their projection fibres to the distributers, while the higher psychical region is the suzerain or director of the entire business.

My objects in this paper are (1) to present succinctly a series of personal observations, some already recorded, and others not, demonstrating the existence of the centres of the zone of language according to the exposition just made, in this connection giving some corroborative proofs, although any extensive study of the enormous literature of the subject will be avoided; (2) to show by personal clinicopathological cases, with necropsies, the correlations of the zone of language with the sensory and motor spheres of the brain; and (3) leaving clinicopathological facts, to give briefly the biological principle which is fundamental to our conception of the speech zone and its subdivisions. That a discussion such as is intended in this contribution is called for at this time is evidenced in the first place because the extent and the particular subdivisions of the zone of language are still matters of dispute among those who have paid particular attention to cerebral speech. As high an authority in neuroanatomy and in clinical neurology as Dejerine, for example, still contends that a graphic centre in the second frontal gyre does not exist, holding that Broca's convolution is sufficient for all the purposes of the arrangement of language both for articulatory expression and for writing. The question of a naming centre may be regarded as still under discussion. Another matter of some interest and of some uncertainty is the exact part played by the subfrontal gyre and the insula respectively in the mechanism of language, whether, for instance, these parts represent stages in the evolution of cerebral language or whether they act conjointly as one centre. The writer has had the unusual opportunity of observing clinical cases with necropsies and in some instances cases operated on by surgeons, which demonstrate every localization given in the zone of speech as here delineated and discussed. In presenting these cases I shall condense as much as possible, being desirous only of enforcing particular views without going into cumbersome details. References made to cases hitherto recorded will be especially brief. It will appear that however much I may have used the work of others in arriving at conclusions regarding the part played by the cerebrum in the faculty of speech, I have in every case been able to confirm the positions adopted or assumed by personal experience. In taking up the discussion of the different centres I shall proceed in part chronologically and in part in obedience to the natural development of the subject, first directing attention to the speech centre which has been longest known and is in most respects at least of greatest importance, that which is, in the writer's opinion, located conjointly in the subfrontal convolution and in the insula.

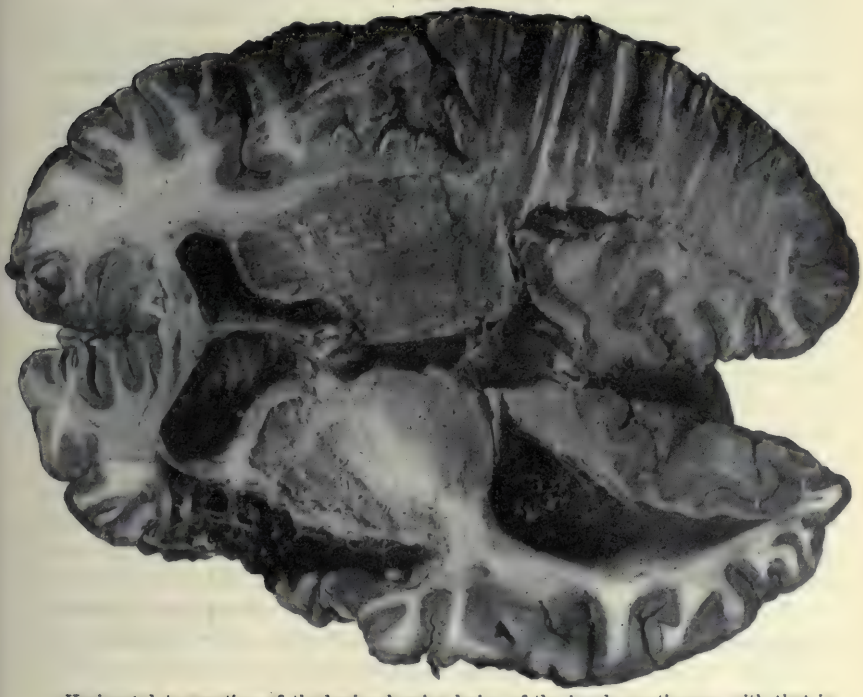
Two photographs (Figs. 3 and 4) are given of a case which has scarcely been exceeded in value in corroborating the existence of a

FIG. 3.



Lateral aspect of the left hemicerebrum, showing one portion of an old lesion circumscribed to the hinder part of the third convolution.

FIG. 4.



Horizontal transection of the brain, showing lesion of the insula continuous with that in the third frontal convolution indicated in Fig. 3; also atrophy of the entire left hemisphere, with enlargement of the ventricles.

centre or area of representation of speech in the caudal portion of the third frontal gyre and in the insula. Gordinier has referred to this case in one of his papers on agraphia, but without illustration, a photograph of the exterior of the left hemisphere and a brief history of the case having been furnished him by the writer.[1] At *A* in Fig. 3 is shown the external portion of an old hemorrhagic cyst, the only lesion related to the aphasia of the patient to be seen on the lateral aspect of the hemicerebrum. It will be observed that this area is strictly confined to the caudal portion of the subfrontal convolution. This brain has been sectioned only recently. A horizontal cut was made at the level of the upper surface of the insula, and revealed the lesion and the appearances shown in Fig. 4. It will be seen that the insula is largely destroyed. This proved on investigation to be a portion or a continuation of the lesion shown at *A* in Fig. 3. In other words, the third frontal gyre and the insula were neatly involved in the same circumscribed lesion, the second frontal convolution, the internal capsule, the basal ganglia, and all other portions of the brain not being the site of any old lesion. Although a section of the brain had not been made at the time of the publication of Dr. Gordinier's paper, his arguments in favor of a graphic centre based on a study of this case remain valid, as the second frontal convolution was not in the least involved.

I made many examinations of this case, and on a number of occasions used the patient at clinical lectures or demonstrations. The case was clearly one of aphasia with marked verbal amnesia and general disorganization of language on its dynamic side. Grammatical expression and combinations were lost. The patient could speak only in single words, or in short phrases, or very short sentences. What he said, however, he articulated and enunciated clearly; he had no paresis of the organs of articulation, enunciation or vocalization.

Besides the old lesion causing the aphasia the necropsy showed several recent hemorrhages—a clot in the left parietal region and two subpial extravasations, one covering the right occipital lobe and another of small size along the longitudinal fissure on the left side about three inches from the tip of the occipital lobe. A glance at the horizontal transection of the two hemispheres shows that the left hemicerebrum is much smaller than the right, the shrinkage appearing to be almost uniform for different regions of the brain. The ventricles and their horns are, however, not only relatively but absolutely larger than on the right side.

This patient, after an apoplectic seizure, developed aphasia, apparently without preceding paralysis or any other symptoms of

[1] Gordinier, H. C. Arguments in Favor of the Existence of a Separate Centre for Writing. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES. September, 1903.

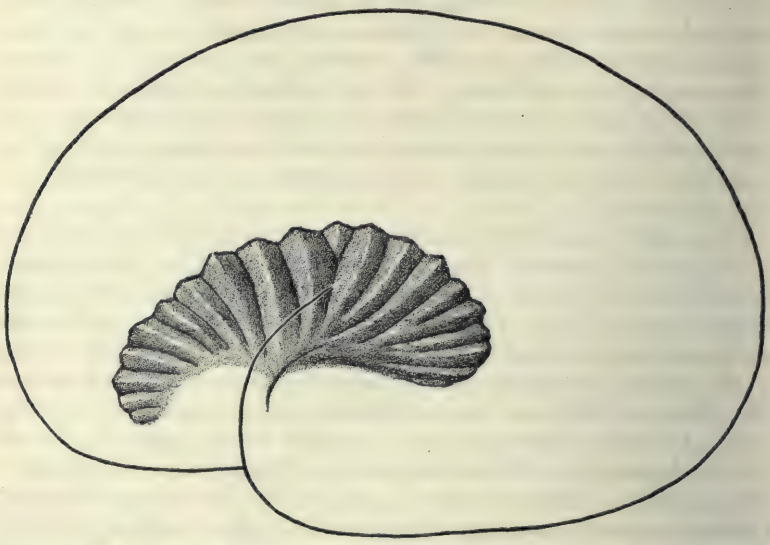
focal lesion like visual blindness and hemianopsia, When examined by me about nine years after the onset of the aphasia, he had almost complete inability to name persons and objects which he was able to recognize through all his special senses. He had also a marked form of paralexia. When he attempted to read, although he understood what he was reading, he repeated an absurd formula of a few phrases. He had limited spontaneous speech, even using short sentences without concrete nouns correctly. He could write many single words correctly, sometimes misspelling, however. He held his pen or pencil correctly and wrote with ease and firmness.

The part played by the insula in cerebral speech has long been a subject of discussion. In accordance with the plan of this paper I shall not go into the literature of the subject, but shall confine myself largely to an expression of personal opinion, giving the evidence for this opinion afforded by my own experience. Some of the most interesting data can be found in works on aphasia like those of Bateman and of Wyllie, and as regards recent literature, particular attention may be called to the paper by Dr. E. A. Spitzka on the "Redundancy of the Preinsula in the Brains of Distinguished Educated Men."[1] Some of the distinguished contributors to our knowledge of aphasia have even gone so far as to regard the insula as the sole cortical centre for speech. This view must, of course, be disregarded in the light of the numerous well-recorded cases of lesion of the subfrontal convolution with aphasia, and also when the numerous cases of degeneration or involution of Broca's convolution after lesion of the temporal lobe are considered. E. A. Spitzka holds that probably only the preinsula is concerned with speech, giving instructive personal observations and a review of the work of others in support of this position. His careful study of the brains of the Seguins, father and son, showed a redundancy of the left preinsula, also that the insulæ were marked by deeper fissures and a complementary plumpness of the gyres compared with ordinary brains. Exposure of the insula is usually regarded as evidence of disease or deficient cerebral organization, but Spitzka shows that this is not always the case, and gives what would appear to be the correct reason for the exceptions. While, on the one hand, deficient development of the opercula causes exposure of the insula, on the other hand in the highly intellectual, and especially in those with an unusual faculty of speech, a displacement and thrusting apart of the opercula also result in insular exposure. Spitzka gives some facts both from comparative anatomy and from an investigation of human brains in support of the view that the caudal portion of the insula has a different function from its cephalic portion. He gives, for instance,

[1] Medical Record, June 15, 1901.

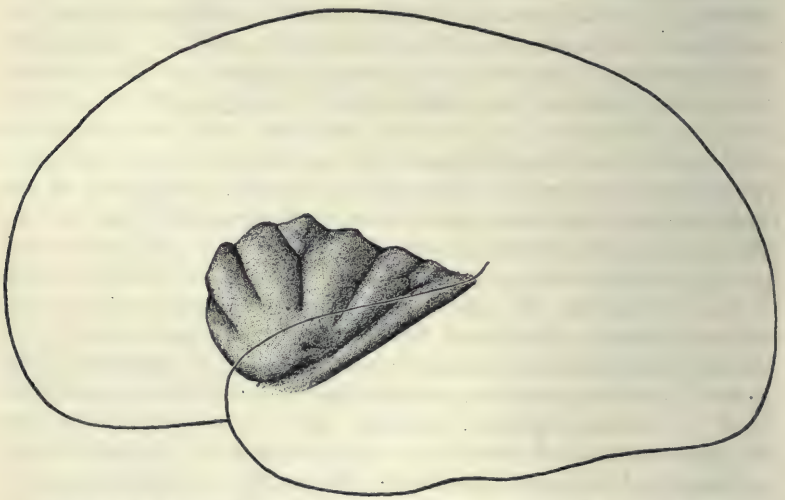
two illustrations, one (Fig. 5) a sketch of the insula of the bottle-nosed dolphin, the other (Fig. 6) of a normal well-developed human

FIG. 5.



Insula of the bottle-nosed dolphin. The caudal portion of the insula of this cetacean is more redundant than the cephalic. The entire insula is large, having, as shown in the diagram, as many as eighteen fissures and nineteen gyres. (E. A. Spitzka)

FIG. 6.



A normal well-developed human insula, showing that relatively the cephalic is more developed than the caudal portion of the insula. The number of fissures and gyres, as will be seen, is less than one-half as great as that in the dolphin. (E. A. Spitzka.)

insula. The differences are striking. In the case of the dolphin the fissures number about twenty, while in that of the man they number five main fissures, two of these being subdivided. The gyres of the preinsular portion of the dolphin's insula are relatively small, while the reverse is the case in the human insula. It seems to me that much is in favor of the view that the preinsula is particularly concerned with speech. Up to the present time the students of cerebral morphology, anatomy, and physiology have not succeeded in locating with any certainty the cerebral terminus of the vestibular portion of the eighth nerve, although the writer has indicated it tentatively as probably being in the second frontal gyre. It may

Fig. 7.

Photograph of the insula of a man of average intelligence without brain disease.

be that the postinsula is related to the cortical centre of representation of the vestibular nerve as is the preinsula to the auditory centre. Spitzka regards the preinsula as an association area for speech, a cortical region which unites the sensory side of the zone of language or a portion of it with the subfrontal gyre, which he speaks of as the emissary speech centre. The writer's view is somewhat different, if he understands correctly the position of Spitzka. I believe that Broca's convolution and the insula (or perhaps only its anterior portion) constitute conjointly the same speech centre, a large cortical area being requisite for that portion of the mechanism of speech which is represented by this region. Neither of these areas has, I believe, projection fibres. Here language is organized for the use of the executive centres concerned

with speech, in other words, for the facial, lingual, and laryngeal centres situated anterior to the foot of the central fissure. This view is similar to that of Clozel de Boyer.[1] The specimens from the first case recorded in this paper (Figs. 1 and 2) support this contention, as when a circumscribed vascular lesion, either occlusion or hemorrhage, is limited to a certain area, it usually follows that the area affected has the same function. It is probable that the most important portion of the middle association area in the zone of language is situated in or near the midtemporal region, probably occupying portions of the second and third temporal gyres.

In one sense the insula and subfrontal gyre are undoubtedly association areas, but in them, to use the idea suggested by Broad-

FIG. 8.

Photograph showing the insula of a speechless idiot.

bent, language is organized into propositions. They constitute conjointly what might be termed a language-arrangement centre, but another association area concerned with the attachment of names to concrete concepts is probably situated in the temporal lobe.

In Fig. 7 is shown a photograph of the insula of a man of average intelligence, but not well educated, the opercula being pulled aside in order to focus the island. In Fig. 8 is given a view of the insula of an idiot.

In Fig. 9 is exhibited the insula of a well-known case recorded in 1891 by the writer, which helped to fix the position of the centre

[1] Thèse de Paris, 1879, cited by E. A. Spitzka, Medical Record, June 15, 1901.

for word-hearing opposite the caudal extremity of the Sylvian fissure at the junction of the first and second temporal convolutions. The illustration shows extreme atrophy of the first temporal, retro-insular, and Broca's convolutions, with almost full exposure of the insula. In the light of what has already been said, these illustrations need but little comment. In the case of the man whose insula is shown in Fig. 7 no affection of language was present, the patient dying from spinal injury and its consequences; the idiot never acquired any power of speech, while the patient from whom the specimen represented in Fig. 9 was taken became word-deaf

FIG. 9.

Photograph of the insula of a case of lesion demonstrating the centre for word-hearing and the general auditory area. The original lesion was at *A*. The first temporal, retroinsular, and subfrontal gyres are much wasted. The first temporal convolution of the right hemisphere of this brain, with other parts, was also destroyed nine years before death by a second apoplectic attack, the first seizure causing the lesion at *A* having occurred fifteen years before death.

fifteen years before death, and nine years later totally deaf cerebrally because of a second destructive lesion of the right first temporal convolution and other parts.

The writer has long believed in the existence of a separate graphic or writing centre situated in the second frontal convolution, and has recently had the opportunity of obtaining new evidence of the most positive character supporting this view. Two classes of cases may be regarded as proving the existence of such a centre, namely, (1) cases in which a lesion absolutely circumscribed to Broca's convolution, or the insula, or both, causes aphasia without agraphia, and (2) cases in which a lesion circumscribed to the alleged position

of the graphic centre in the second frontal convolution causes agraphia without aphasia. I have had the opportunity of personally seeing two such cases. The case illustrated by Figs. 3 and 4 is, in fact, such a case, and I shall make no further reference to it, except to re-emphasize the statement that the patient was an aphasic but not an agraphic.

Recently in a case seen in consultation with Drs. J. W. McConnell, W. G. Spiller and C. H. Frazier, the existence of a graphic centre or motor graphic centre, as it is usually described, was positively demonstrated. The case had many other interesting features. It was one of tumor, largely prefrontal, removed successfully by Dr. Frazier at the Hospital of the University of Pennsylvania. I shall not go into details of the case, as I do not wish to forestall its fuller presentation by others, but shall, with their permission, call attention to the bearings of the case upon the question of the existence of a writing centre. The patient, a man twenty-nine years old, was first affected with a peculiar form of spasm attacking the face and head five years before coming under the observation of Dr. McConnell. Omitting all details of his history and the study of his case except in so far as it related to his agraphia and his mental condition, it may be stated that for over two years he had been changing in disposition and failing in intelligence. A portion of a letter written by him in 1902 shows some omissions of words and faults of spelling and construction, the same words in other parts of the letter being spelled correctly. These mistakes probably indicated the beginning of his agraphia. His recent letters were almost unintelligible. In consultation with Dr. McConnell I examined this man as regards his power to write, the day before the operation.

All attempts to write, either spontaneously or from dictation, were absolutely futile, although he held and handled his pen and pencil properly and copied a sentence with comparative ease. Illustrations of his efforts to write his own name and other expressions will be given in the full account of his case. The patient was not an aphasic. He had considerable difficulty in articulating and enunciating, particularly for a short time before the operation, but numerous tests showed that this was due to paresis of the organs concerned with articulation and enunciation, and was in no sense an aphasia such as results from a lesion of the subfrontal gyre and insula, such, in other words, as was exhibited by the patient from whom the specimens shown in Figs. 3 and 4 were taken. The tumor in this case lay athwart the second frontal convolution exactly in the position indicated in Figs. 1 at *G* and in Fig. 2 at the position marked writing. The reader interested in the subject of motor agraphia is referred to the papers of Gordinier.[1] One case

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, September, 1903.

recorded by Gordinier is an almost perfect demonstration of the existence of the graphic centre.

Confusion still exists in the minds of many as to what is meant by the cerebral motor speech centre. Some, for instance, would make it include both the caudal portion of the third frontal gyre and the centres at the foot of the central or Rolandic fissure. As has already been indicated, the speech centre proper is circumscribed to the subfrontal convolution and insula. Here language is arranged for outward projection. Short association fibres connect this region with the true motor centres for articulation and enunciation, which constitute together the utterance centre or executive speech centre. Numerous physiological and clinicopathological facts and psychological principles could be readily adduced to uphold this view, but, following the plan of the paper as outlined, I shall content myself by referring to a single personal case and to one or two experimental observations. In 1889 I reported a case of paralysis strictly limited to the tongue, lips, and lower face, with slight implication of the palpebral orbicular muscle of the same side. Speech was entirely unaffected except as regards the effect on articulation caused by the lingual, oral, and slight facial paresis. The necropsy showed cortical softening involving the lower extremities of the central convolutions both on the lateral and Sylvian surfaces, and a spot one-half an inch in diameter about the middle of the internal portion of the insula. The softening reached into both the central and the precentral fissures. The anterior limit of the softening was one-fourth of an inch back of the anterior branch of the Sylvian fissure. This case seemed to clearly indicate that the true speech centre was confined to the subfrontal convolution and a portion of the insula, the area for the tongue, face, and allied movements being in the inferior portions of the central convolutions and largely in the precentral. In recent years I have come to believe that the motor region lies entirely or almost entirely in front of the central fissure. If there is any exception to this in the case of the human brain it is probably with regard to the centres for articulatory and allied movements. As is well known, the central fissure in the human cerebrum is only confluent with the Sylvian in extremely rare cases, and the entire gyral mass which separates its lower extremity from the Sylvian fossa may be concerned with movements which pertain to articulation, although by far the largest portion of the motor region, even in this position, is probably cephalad of the central fissure.

Grünbaum and Sherrington[1] found that unilateral faradization of Broca's convolution in the anthropoids evoked no movement, and in one case observed by the writer, faradization of the human

[1] Proceedings of the Royal Society of London, November 21, 1901; February 27, 1902, May 25, 1903.

subfrontal during an operation gave similar negative results, although in the same case the application of the electrode to the centres of the face, eyelids, and head gave prompt and positive response.

It is not necessary to record here cases of lesion of the area for the upper extremity (*WM*, Fig. 1), or its subdivisions, without involvement either of speech or writing. Such cases with necropsy have been seen by me, and a considerable number have been put on record. They simply show, as other cases referred to in this paper when discussing the writing centre, that the region of representation of the organization or arrangement of language for writing is independent of the area of representation of the movements of the upper extremity.

I shall make only brief reference to the auditory centre for speech, more commonly designated as the word-hearing centre. This is located at about the position *WH* in Fig. 1 and at that marked word-hearing in Fig. 2. As will be seen from a study of the diagram Fig. 2, the writer's present views with regard to auditory, visual, and concrete concept representation make it necessary to look upon some of the questions of speech localization, as of other forms of functional representation, somewhat differently from the manner in which these subjects have been hitherto regarded. In the cerebral cortex are situated primary auditory and primary visual centres, and, indeed, primary centres for all of the forms of sensibility, special and more general, as for cutaneous sensibility, smell, and taste. Each of these centres has surrounding it what may be termed its sphere of influence, this in the case of the auditory centre being a large area concerned with all forms of what in a broad sense might be termed object-hearing. Within this general region of special sounds-recognition are probably located a separate centre for natural sounds, like the notes of birds, another for musical notes, and still another for word-hearing. The centre of primary recognition is probably located, as represented in the diagrams Figs. 1 and 2, in the caudal portion of the first temporal gyre and in the retroinsular gyres. The word-hearing centre is on the outskirts of this region, at about the junction of the first and second temporal convolutions. It is not necessary to reproduce the evidence of this localization, which has been accumulating for years, and especially since Wernicke's first thorough presentation of the subject in 1874.[1] No more convincing case indicating the localization of this centre has been presented than that reported by the writer[2] in 1891. This case is now well known, and has been referred to in various articles and treatises. The illustration Fig. 9 is from a photograph of the left hemisphere of this case. From a study of the lesions

[1] Der aphasische Symptomcomplex, Breslau, 1874.
[2] University Medical Magazine, November, 1891.

found in this brain I concluded that the centre or area for word-hearing was situated in the caudal thirds of the first and second temporal convolutions, the focus of the area being about in a line with the extremity of the Sylvian fissure.

Built up by processes of education and through heredity, visual centres for numbers, letters, and words have developed out of a general area for object-seeing in that portion of the brain usually designated as the angular gyre (at the positions indicated by *WS*, *LS* and *NS*, Fig. 1, and by the terms word-seeing, letter-seeing, and number-seeing, Fig. 2). The evidence in favor of this highest visual area is of such a positive character and so well known that it is not necessary to adduce it in this paper. I would simply say that during the last two to three years I have had further corroboration of this localization in cases of brain lesion for which operations have been performed. In one of these cases the existence of a centre for object-recognition, independent of that for the recognition of words, letters and numbers, was indicated by attacks of transient mind-blindness, the lesion in this case probably occupying portions of the second, third, and perhaps of the fourth occipital convolutions. At the point marked *N* in Fig. 1, and naming in Fig. 2, is probably located a special region where names are correlated to the concrete ideas of objects which are recognized by sight, hearing, or other senses, or through the interaction of the centres of these senses. While the separate existence of this centre may be regarded as not absolutely settled, I believe the weight of evidence and of *a priori* considerations are in favor of its existence. From the nature of the work which it is supposed to do its situation should be related more closely to the sensory than to the motor side of the brain, and a portion of the third temporal convolution, or of this and a portion of the second temporal, as indicated in the diagrams, would seem to be its probable location. Some clinicopathological facts also point to this conclusion, as, for instance, a case described by the writer and McConnell, and others recorded by German observers. The reader interested in this subject is referred to the writer's articles on aphasia in his work on *Diseases of the Brain*,[1] and to a paper published in 1902.[2]

The correlation of the cerebral zone of speech with the sensory and motor regions of the brain is illustrated by those cases of mixed sensory and motor aphasia which are not infrequently observed. A common symptom-complex is that of nearly complete right-sided hemiplegia with correspondingly almost complete aphasia. Two or three such patients presenting this syndrome are usually to be found in the wards for nervous diseases of the Philadelphia Hospital—the hemiplegics with a single recurring

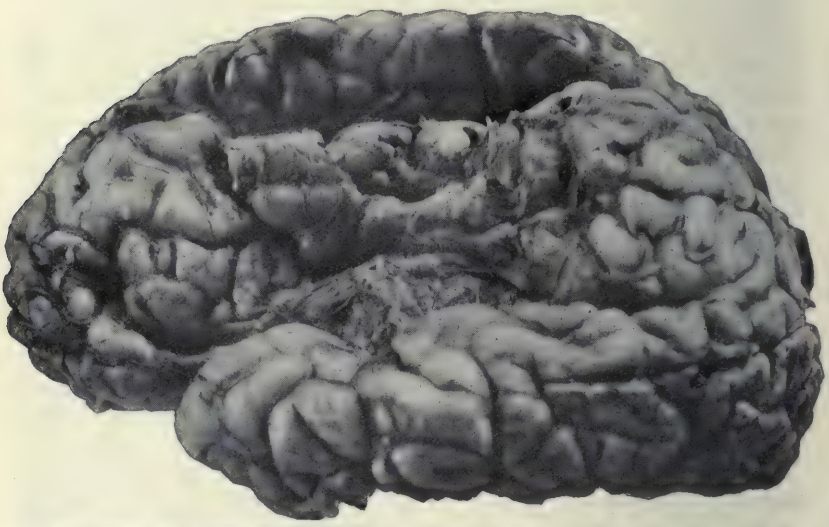
[1] The Nervous System and Its Diseases, Philadelphia, 1898.

[2] Journal of the American Medical Association, October 4, 1902.

utterance or with only one or two such utterances. The photograph of a specimen recently obtained from such a case is shown in Fig. 10. The case is identical in most respects with one reported by Burr.[1]

My patient was for many years in the Philadelphia Hospital, and was frequently used by me and others to illustrate lectures and demonstrations of aphasia. She was one of a group of cases studied by me with reference to pantomime as well as speech, and a clinical report of the case was made in Vol. II. of the *Philadelphia Hospital Reports*, published in 1893, the patient living eleven years after that time, but not changing in any essential particulars until her last

FIG. 10.



Photograph of the lateral aspect of the left hemicerebrum of a case of hemiplegia and complete aphasia, the apoplectic attack having occurred between fourteen and fifteen years before death. All parts of the brain supplied by the left medicerebral artery are necrosed.

illness. She was about fifty-one years old at the time of her death. Fourteen or fifteen years before her death she had an apoplectic seizure causing loss of power in arm, leg, and face, without aphasia; a few months later she had a second seizure, causing profound hemiplegia with contractures and aphasia. Sensation, so far as could be determined, was unimpaired. The deep reflexes in both upper and lower extremities were exaggerated on the paralyzed side. It was impossible to learn whether or not the patient was word-blind in the absence of her previous history. She was largely but not completely word-deaf. She was not mind-blind. "Her speech and pantomime," citing from the *Philadelphia Hospital*

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, February, 1904.

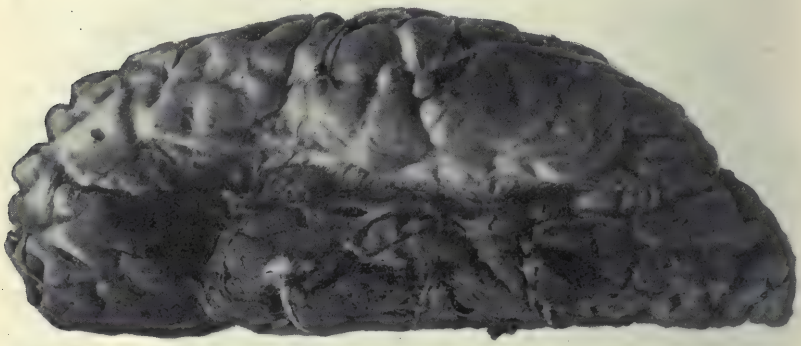
Reports, "might be said to be summed up in her *la-la* and laugh and a much less frequent expression of anger or displeasure, which was usually accompanied by a movement of covering her mouth with her hand. The appearance of her face could not be said to be without expression, but, like her recurring utterance, it was an appearance nearly always the same. It might mean that she was pleased and it might signify assent or dissent; it might mean anything at all. Sometimes the *la-la* and the laugh became louder and more emphatic, but that was all. She never nodded the head in the usual manner for *yes* or *no*." This patient died in 1904, during the term of service of my colleague, Dr. C. W. Burr, to whom I am indebted for the opportunity of obtaining the results of the necropsy, the record of which will be omitted except as regards the brain.

Examination showed that the left medicerebral artery was occluded near its origin from the internal carotid, and necrosis of all parts supplied by the branches of this vessel had occurred. The first temporal convolution, the insula, the subfrontal, precentral, postcentral and inferior parietal convolutions were all necrosed and atrophied, as were also the ganglia and capsules and corona radiata, in so far as these are supplied by the branches of the medicerebral artery distributed to the interior of the brain. The left hemisphere was greatly reduced in bulk and had the appearance of being caved in between the prefrontal and occipital regions. The external appearances are shown, although not particularly well, in Fig. 10. The whole hemisphere is greatly reduced in size, as shown both externally and in a horizontal section made at the level of the insula. The parts necrosed included the entire motor region and its environing sensori concept motor speech zone, and in addition, large regions of the ganglia and capsules at the base. The lesions found in this case, as in that of Burr, are probably those usually present in cases of complete aphasia with a hemiplegia also nearly complete.

In some cases the aphasia is as nearly total as in the case just recorded, the hemiplegia being absent or represented only by an incomplete hemiparesis. In Fig. 5 is shown the photograph of the brain of such a case. This patient, like the one just recorded, was for many years a well-known character at the Philadelphia Hospital. Just as the other patient was frequently spoken of as *la-la*, so he came to be known as *anyone any*, this being his single recurring utterance. The history of the case is unfortunately lost, but the patient was well known to me, and was frequently used by me in clinical lectures and demonstrations. He was slightly paretic on the right side, but to so small a degree that he was quite useful as an assistant in one of the kitchens of the hospital, where he long worked. He was partially word-deaf. It is probable that he was completely word-deaf at first, and had to some extent recovered

word-hearing power. He was very acute in observing others when they were speaking, apparently sometimes recognizing what they said by the movements of articulation. To everything that was said to him he would simply answer *anyone any*, yet his appearance and manner sometimes indicated that he knew what was said, his knowledge evidently being obtained partly by sight and partly by hearing. His pantomime was not nearly as much disturbed as in the preceding case. Necropsy showed the conditions indicated in Fig. 11. The main trunk of the left medicerebral artery was not completely closed as in the preceding case, the branches occluded being those distributed to the insula and to the opercular convolutions, the third frontal, central, subparietal, and first temporal; those convolutions were so necrosed as to be almost obliterated.

FIG. 11.



Photograph of the left hemicerebrum of a case of complete aphasia with right hemiparesis. The subfrontal convolution, the insula, and the first temporal convolution and adjoining parts are completely destroyed.

It has seemed to me worth while to record the cases contained in this paper and at the same time to glance at the entire subject of the cerebral zone of speech, with the view of clearing up some disputed points and emphasizing others. The acquirement of speech is the first great step in the separation of man from animals lower in the scale. Man differs from the gorilla chiefly in his ability to talk and in being better looking. Relatively the brain of the gorilla and of the other anthropoids shows lack of development in the region given over in man to the zone of speech, while in these animals the primary centres for vision, audition, and movements are largely developed. The centres for word-hearing, word-seeing, for speech-associations and for writing have developed in the race and in the individual as these functions or attributes have been added to man's resources for communicating by language with his fellows. It is well that the students of comparative and of human anatomy and physiology, that clinicians and path-

ologists, should spend much time and labor in determining the existence and in accurately locating the various centres of representation in the zone of language, but the existence of these centres is ordained by evolution. The position, the size, and probably the shape of the cortical areas which are spoken of as the centres concerned with speech are determined by unalterable biological principles. The anthropoid and the human savage alike have large cerebral areas for object-recognition, whether through sight, hearing, touch, or the other senses. As man learns to talk the auditory speech area or centre develops in close proximity to the regions of primary representation of sound. Similarly, centres for visual speech develop within the sphere of influence of the primary visual centre, and the areas of language arrangement both for speech and writing in proximity to the great motor area, parts of which become the final cerebral instruments of speech. It is just as necessary that the man who writes spontaneously should have a centre for language arrangement for writing as that he should have a similar centre for speech, and the same is true of every subarea so far determined in the great zone of language. With our present knowledge of cerebral structure and function it is just as certain that a separate graphic centre or a separate centre for word-hearing or for word-seeing has its place in the human cortex on the principles here enunciated, as appears from the records of convincing clinicopathological cases by Broca, Gordinier, Eskridge, Dejerine, Wernicke, or anyone else.

TRAUMATIC HEMORRHAGE OVER THE THIRD ANTERIOR FRONTAL CONVOLUTION; OPERATION; REMOVAL; RECOVERY; REMARKS ON PRESENT STATUS OF BRAIN SURGERY.[1]

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The surgical invasion of the brain begun so auspiciously under the leadership of the English surgeons Horsley and MacEwen, has not proven so successful as the first reports seemed to indicate; nevertheless immense strides have been taken in this direction, and beneficial results have been obtained in a once barren and hopeless field.

[1] Read at the Ninety-eighth Annual Meeting of the Medical Society of the State of New York, January 26, 1904.

Tumor, abscess, hemorrhage, epilepsy, microcephalus, insanity, and the removal of the Gasserian ganglion for tic douloureux are the indications most frequently calling for surgical intervention, and the trephine has become an all-important agent in the treatment of these various lesions. The success in any of these conditions depends upon (1) an accurate diagnosis made early in the course of the disease; (2) an accessible lesion demanding the minimum of brain destruction; (3) a faultless surgical technique.

With these conditions anticipated and overcome, results will follow which will restore to brain surgery much that has been lost by indiscriminate surgical meddling which marked the early period of this procedure. Up to January 1, 1903, Starr[1] found in medical literature 365 cases of brain tumor operated on, 315 being cerebral and 50 cerebellar, with the following results:

	Total.	Cerebral.	Cerebellar.
Cases in which the tumor was *not* found	111	91	20
Cases in which the tumor was found, but *not removed*	27	21	6
Cases in which the tumor was removed and the patient *died*	59	51	8
Cases in which the tumor was removed and the patient *recovered*	168	152	16
Percentage of failures	38		
Percentage of deaths	16		
Percentage of recoveries	46		

These figures are sufficient to give confidence and to stimulate further efforts in this direction.

Woolsey,[2] in an instructive paper on the surgery of cerebral tumors, including a table of 101 cases of cerebral tumors, emphasizes the following conclusions: 1. The sphere of operation for cerebral tumors may be and has been extended to those parts of the cortex where tumors are accessible and localizable—*i. e.*, to the prefrontal, parietal, and occipital regions, in addition to the motor area. 2. The prognosis, both immediate and remote, is as good or even better than in operations for malignant growths in some other locations. 3. This prognosis has improved with the improvements in localization and operative technique, and with the limitation of the radical operation to cases accurately localized. 4. The palliative operation is strongly indicated to relieve symptoms where localization cannot be accurately made or the tumor cannot be removed. The exploratory operation is contraindicated. 5. Practically all circumscribed growths of moderate size are suitable for operation. 6. The osteoplastic method should be employed and the most rapid and perfect technique adopted which the circumstances allow.

The application of surgery for the relief of traumatic insanity and traumatic epilepsy has not been as favorable as anticipated,

[1] Journal of Nervous and Mental Disease, July, 1903, p. 398.

[2] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, vol. cxxvi. p. 956.

and operations for these conditions are becoming justly less and less. In 33 cases of epilepsy operated on at the Craig Colony, Sonyea, N. Y., Dr. Spratling[1] noted the following results:

In 21 there was no improvement in the disease, either temporary or permanent. In 8 the attacks were lessened in frequency and severity, the operation being a part of the treatment only. In 3 the disease was much worse after the operation. In 1 there was apparent recovery.

The writer reported a case of traumatic epilepsy[2] operated upon May 2, 1891, with freedom from attacks for twelve months, then recurrence. A second operation on October 15, 1892, with freedom from attacks for three years; a third operation was performed in 1895, with favorable results for three years, and finally the attacks becoming again so frequent a fourth operation was carried out November 25, 1902, and the patient died from the shock. The opening in the skull measured four inches in diameter. In idiocy and imbecility with microcephalus, brain surgery has been most disappointing. Starting with the enthusiastic report of Lannelongue in 1891, the early reports looked favorable. As time went on the successes were less frequent and to-day the operation is rarely performed except where there is simple development and not where extensive lesions exist (Dana).

Spratling[3] presents 194 such cases in the paper referred to under two heads in condensed form, the first group including the more immediate results in 111 cases, with the following results:

Died in consequence of operation or soon after	19 or 17 per cent.
Operated on with no result	25 or 22.5 "
Operated on with slight result, but not satisfactory	10 or 9 "
Improved in stated ways	24 or 21.5 "
Improvement without reports as to its character	30 or 27 "
No reports as to results given in general	3 or 3 "

The second group of 83 cases with results somewhat more permanent was as follows:

Died	20 or 24 per cent.
Unimproved	54 or 65 "
Improved	9 or 10½ "

Lowenstein voices, perhaps, the popular notion regarding this operation: "With the hypothesis of the primary synostosis of the sutures and fontanelles and the secondary hindrance of brain development stands or falls the right of Lannelongue's operation. The hypothesis is false and therefore the operation is not a suitable one. Death or no results follow."

The Krause-Hartley operation for the removal or breaking up of the Gasserian ganglion in cases of obstinate facial neuralgia

[1] American Journal of Insanity, July, 1903, p. 27.
[2] Buffalo Medical Journal, November, 1895.
[3] Loc. cit.

has been measurably successful and continues to receive attention. Two cases recently presented before the Buffalo Academy of Medicine by Drs. Marcel Hartwig and William C. Phelps were entirely relieved of their torture by this operation.

Perhaps the most favorable field for the trephine is in cases of subdural hemorrhages due to traumatism or to spontaneous ruptures during violent spasmodic seizures, as in whooping-cough. These hemorrhages, whether extradural, subdural, or cortical, fall within the jurisdiction of the surgeon, and as a rule, if operated upon early, give very gratifying results. Whether or not these hemorrhages would absorb without operation depends upon the extent and source of the hemorrhage; the surgeon no doubt in some cases does no more than hasten what would naturally have occurred.

Success in cases of hemorrhage, as in brain tumors, also depends upon an early diagnosis, a correct localization, and a faultless surgical technique. The following case of *contre-coup* hemorrhage due to traumatism is deserving of publication, and resembles in some respects the case reported by Starr in *Brain Surgery*, 1893, p. 161. As in that case, so in the one to be reported, a complete recovery followed the removal of the clot.

L. B., male, aged sixty-two years; height, five feet eight inches; weight before accident, two hundred and two pounds; constitution strong, vigorous; heavily built man. He had always enjoyed the best of health, had never contracted syphilis, but for years had been moderately addicted to the use of liquor.

On Monday evening, August 10, 1903, at about 7.30 o'clock, while trying to pass from the rear platform of an open trolley car along the running board to a seat, he stumbled against the wheel guard and was precipitated to the pavement. The car was running at a speed of perhaps five miles per hour, and he struck the asphalt pavement on the right side of the head, over the region of the right eye, and in trying to save himself struck on his right shoulder and right hand. As a result of the fall he was somewhat stunned, but declared to Dr. Pfohl, who was on the car, that he was "all right" and not injured to any extent. He was driven to his home accompanied by the doctor, who found the following condition:

The right eye was greatly swollen and discolored; the upper eyelid stuck out like a cup; the conjunctiva was greatly ecchymosed, overlapping the cornea, and the eye was practically closed by the effusion. The right shoulder was bruised and discolored, and one of the metacarpal bones of the right hand was fractured. He complained of great pain over the occiput during the night, of such intensity that the neighbors were disturbed by his cries and groans. He had eaten a hearty supper that evening and vomited at intervals throughout the night.

The following day, Tuesday, he was more or less under the influence of narcotics, but vomited occasionally. He conversed

with his wife and daughters on various topics and appeared to be recovering rapidly from the fall. His son, a careful observer, visited him at noon on Tuesday, and with the exception of the discoloration noticed nothing wrong about him. He talked about the accident and business matters, and when asked if his employés should be notified said, "No, I will be out in a few days." At 11 o'clock that night he was sitting up with his family, reading the newspaper and engaged in general conversation. He slept fairly well Tuesday night.

On Wednesday morning, August 12th, at 6 o'clock, his wife approached his bed and asked if there was anything he wanted, to which he made an unintelligible reply. Thinking he was jesting his wife asked, "What language are you talking, Italian or Polish?" He evidently did not recognize her, but kept on jabbering in an unintelligible and incoherent manner. To his sister, who visited him this morning, he said, "Hello, Clara!" very plainly, then jabbered for some seconds.

Wednesday noon his son called again, and to the question how he felt replied, quite distinctly, "All right." On attempting further conversation with the father the son noticed that the first two or three words of a sentence would be distinctly spoken and the remaining words would be an unintelligible jumble, as if spoken in a strange language. As time went on the distinctly spoken words became less and less and conversation was stopped. During the day he grew more confused; became partially unmanageable; insisted on going to the toilet room; refused all nourishment; left the bed several times, and tried to clothe himself. Being a strong, powerful man, he was unopposed in his desires and actions. He did not complain of any headache and had not vomited this day. The case having assumed a more serious aspect, Dr. Marcel Hartwig was called into consultation. The following day, Thursday, August 13th, I was asked to meet Drs. Pfohl and Hartwig in consultation.

The patient was in bed, but during my stay at the house arose twice and, slightly assisted, went to the toilet room at the other end of the house. He did not show any peculiarity of gait, did not stagger nor go sideways, and did not fatigue perceptibly by the exertion. He would not use the bed-pan, and although recognizing the danger of further hemorrhage, still we did not deem it wise to force matters with him.

His face was badly disfigured and discolored, especially about the region of the right orbit. He did not seem to know me or to appreciate his surroundings. He was stuporous, breathing heavily, his cheeks ballooning in expiration, and only with difficulty was his attention riveted for a few moments. He did not reply to questions put to him, and only once did he mutter something in reply to Dr. Hartwig.

There was no paralysis of the facial muscles, or of the arms or legs; neither was there any tremor or twitching of any of these muscles. Pupils equal and react to light. The tendon reflexes and deep reflexes were normal, and no disturbance of sensation.

The pulse was 72, temperature 98.5° F., and respiration 20. The following day, Friday, found him in practically the same condition, perhaps somewhat more stuporous and a temperature of $100\frac{4}{5}$° F. in the morning and $101\frac{3}{5}$° F. at 6.30 P.M. He drank milk and water freely, and did not complain of headache. Early in the evening his son noticed a slight tremor of the chin and later on the family observed that at frequent intervals he would without moving his head slowly turn his eyes toward the right. They thinking he was annoyed by a picture on the wall removed it, but it had no effect on the patient. At times his lips trembled and he uttered a cry like "mum, mum, mum." The nurse had been instructed to watch the right arm carefully for twitchings or contractions and to report at once their appearance.

At 10.40 Saturday morning the nurse noticed that the patient would have convulsive seizures of the right side of the face instead of the arm, becoming more and more frequent, and at once telephoned for the physicians. Arriving at the house I found Drs. Hartwig and Pfohl, who had been eye-witnesses to several of these attacks, and it was not long before another one made its appearance.

The patient was lying on his back quietly, then slowly moved his head slightly toward the right. The eyeballs in turn moved toward the right and then the eyelids were closed. This spasmodic action lasted but a few seconds and was followed by a series of clonic convulsions. The forehead was not involved except by transmission. The whole right face moved up and down convulsively; the mouth was drawn to the right, and the jaw worked in unison with the face. A peculiar sound was made by the working of the lips, as if smacking, and the tongue could be seen between the teeth jerking and pointing toward the right. The right pupil was dilated, but as the left eye had been atropinized the day before no comparison of the two pupils could be made.

Following the clonic seizure, which lasted perhaps thirty seconds, the patient resumed his normal appearance and breathed heavily for a few moments. There was no involvement of the right arm or leg, no foaming at the mouth, and no involuntary urination.

It was now definitely decided to urge upon the family the necessity of an immediate operation. Consent having been willingly given, it was decided to operate at 3 o'clock that afternoon. While this conversation was going on in the sick-room, unfortunately the patient overheard and understood its full import, as he was seen to cry, and sobbed for some time. He assisted in dressing himself, and on looking out of the window and seeing the ambulance before the house, said very plainly, and distinctly, "No hospital for me."

He was greatly agitated and aroused and fought all efforts to go. A carriage was thereupon ordered and it was thought he might be induced to enter under the guise of going for a drive; but he waved his hand and said again, very distinctly, but pitifully, so that all in his vicinity could hear him, "You can't fool me." He was then forcibly picked up, carried into the ambulance, and hurriedly driven to the German Hospital.

Surgical Report by Dr. Marcel Hartwig.

Concerning the surgical features of this interesting case, which is the second in my experience, there is not much to be said. *Contrecoup* bleedings are frequently due to ruptures of the arteria meningea media or its branches. In this case I could not establish this fact, although the quantity of blood clots between pia and dura amounted to about three teaspoonfuls, and the flow of subdermal blood was considerable. We have, therefore, to conclude that some venæ communicantes were torn, the surface of the brain itself looking too good in the trephine opening to believe that a rupture of the brain itself should have existed in the covered neighborhood. Drainage by two catgut loops, one forward and one backward, inserted respectively one and two inches deep, was sufficient to take care of the leakage after the trephining. A fissure in the bone was not discovered. Healing under the first dressing. The dura was partly united by catgut. The thinned catgut strands were withdrawn on the fifth day. Two convulsive seizures of light type occurred the first night, not to appear again. The skilled assistance of Dr. H. J. Waterman, of New York, was my pleasant privilege to have on this occasion.

Following the operation he had no spasm until 10.50 P.M., when the usual convulsive seizure appeared. This was followed by another seizure at 12.30 A.M. and 1.25 A.M. Sunday. His pulse during the night ranged from 72 to 90, temperature from 103° to 104° F. He muttered unintelligibly during the night, was restless, passed urine involuntarily, and tried to tear off bandages. During the night from Sunday to Monday he uttered many intelligible words, as, "I must go down to the store," and concerning business matters. He made many motions about giving out and receiving money; imagined he was smoking, going through the motions of putting the right hand to his lips and then knocking off the ashes from cigars. The hospital physician noticed some twitching and blinking of the right eye, with some involvement of the face and chin of the right side. These attacks were very slight and lasted only a few seconds. These light seizures, it may here be stated, were the last to be observed, occurring about forty-eight hours after the operation.

Pulse on Monday, August 17th, ranged from 76 to 88, temperature from 102° to 103° F. On Tuesday, the 18th, he spoke at times very plainly, calling for his children and talking at random about his business affairs.

Wednesday, August 19th, the dressings were changed by Dr. Hartwig and showed slight staining with cerebrospinal fluid. No further hemorrhage had taken place. The wound was healing rapidly by first intention, and with the exception of a semistuporous condition at times, the patient was progressing satisfactorily. On being roused he answered questions plainly. For instance he said, "I want a drink of cold water," "I am tired." He asked what time it was, and when told it was 8 o'clock, said, "I want to go to breakfast." Pulse to-day ranged from 80 to 94, temperature from 101° to 101$\frac{3}{5}$° F.

On Thursday, August 20th, he gave his name and address correctly, spelling his name, and spoke quite audibly on being questioned. A mild delirium comes over him frequently during the day, characterized by incoherent language about his business affairs, tearing off bandages, and escaping into the corridors. At night he imagines people looking in through the window. Thinks he is under arrest and offers to settle. He becomes very restless and is with difficulty quieted.

On August 27th the wound had thoroughly healed, the temperature had fallen to 99° F., pulse 72 to 75, and urination ceased to be involuntary. A decided general improvement had taken place in his general condition, the delirium had passed away, and all irregularity of speech had ceased.

On September 2d, 4.30 P.M., the nurse reported as follows: "For the first time as the newspaper was lying on the sofa, the patient reached out and took it. He opened it and read aloud from the first page as correctly and as good as one could ask without glasses."

He wrote some short letters on September 5th, and on the 9th accompanied his wife to the street car.

On September 12th he was dismissed—cured. His urine during his stay at the hospital contained a small amount of albumin.

September 15, 1903, accompanied by his nurse, he reported at my office, when I made the following examination: The flap on the left side of the head has healed perfectly. It is two inches wide at the base and two inches long. The rounded apex is three and a quarter inches above the external auditory meatus. The distance from the upper incision to the external auditory meatus is three and three-eighths inches. The pupils are equal, react to light and accommodation; the fundi are normal; papillæ not inflamed. The two sides of the face are symmetrical and functionate equally; tongue when protruded shows no deviation and the uvula hangs straight. There is no perceptible change in the character or volume of his voice, and he says that friends to-day recognized his voice over

the telephone without knowing beforehand who was at the phone. There is no difference between the sensation of both facial halves. A mental peculiarity still present is his inability to remember names. He forgets name of nurse, of the firms with whom he transacts business, and of old acquaintances. He complains of pain over and about the seat of the wound, commencing over the left eye and travelling backward beyond the scar. He says that before the operation he was very near-sighted, now is much better in regard to vision, and can see to read names across the street. The nurse

FIG. 1.

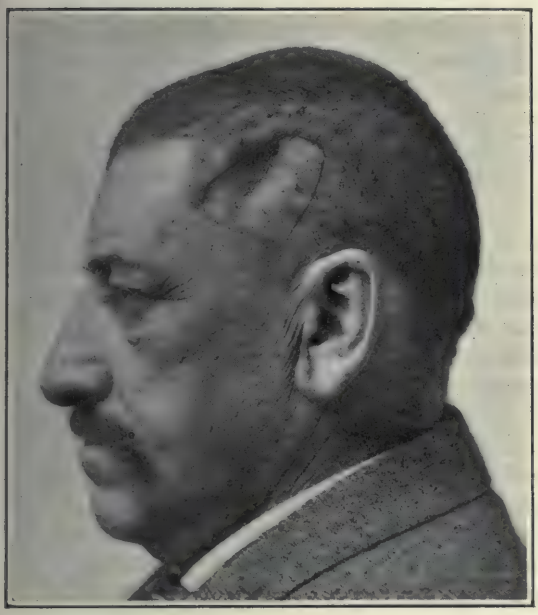

FIG. 2.

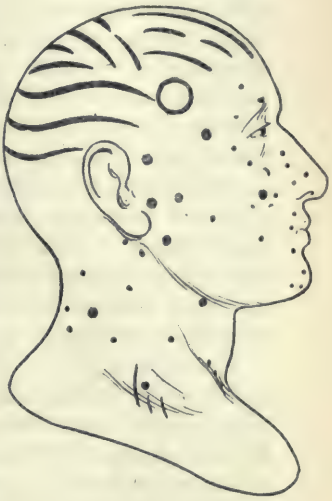

FIG. 1.—Showing the outlines of scalp wound and depression of skull caused by trephine opening, one month after operation.
FIG. 2.—Showing trephine opening and underlying brain convolutions.

was retained for two weeks, during which time the patient's memory returned to its normal, and he began his ordinary routine work the forepart of October, 1903.[1]

The case is a remarkable one in many respects. That a basilar fracture of the skull did not follow the heavy blow of his head on the pavement is unusual. Severe concussion of the brain did not even follow, as he was not rendered unconscious, and said after being picked up, "Oh, I am not hurt much." The pain and attacks of vomiting the following day were the only evidence of any cerebral

[1] June 15, 1904, patient is in every respect in same good health as before the accident.

injury, and were it not for his contused eye and face he would have been at his business on Tuesday, August 11th. What happened was a small localized hemorrhage of the brain membranes on the side of the head opposite to the infliction of the blow, commonly known as *contre-coup* hemorrhage. This occurred immediately over the cap of Broca, third anterior frontal convolution of left hemisphere. The hemorrhage was slowly progressive, as no difficulty of speech was noticed until some sixty hours after the injury, producing symptoms of aphasia and paraphasia. The extension of the hemorrhage backward and downward, involving the facial centre, was no doubt due to the gravity owing to patient's recumbent position. The vessel injured was undoubtedly a small vein of the pia, situated perhaps just anterior to the speech centre, and not producing localizing symptoms until involvement by pressure of the neighboring brain cortex. The slowly on-coming procession of symptoms would vouch for this conclusion, as headache and vomiting the second day, aphasia and paraphasia the third day, and facial epilepsy of the Jacksonian type on the fourth day after the injury. Whether the arm and other centre would have become involved later is questionable. As the dressings on the fourth day after the operation showed no blood stains, only those of cerebrospinal fluid, it is safe to assume that the pressure of the clot upon the injured vessel was sufficient to stay further hemorrhage, and that no other centres were liable to compression. The diagnosis of hysteria was not to be totally disregarded.

The tardy appearance of symptoms after a railway injury, peculiar behavior of patient, his inability to converse or even to utter intelligible words from Wednesday night until he saw the ambulance in front of door, and then distinctly saying, "No hospital for me," and "You can't fool me," could all be easily regarded with suspicion, and the diagnosis of hysteria was never wholly lost sight of until the appearance of the facial epilepsy of the right side. This fact, coupled with the aphasia, showing successive involvement of neighboring brain centres of the left hemisphere, was absolutely conclusive and made the diagnosis unconditional. The finding of the clot with small loss of the calvarium, its speedy removal, the hasty healing of the wound, absence of all sepsis, and complete restoration of the patient to perfect health, all within a few weeks, show surgical skill of marked degree.

THE ADAMS–STOKES SYMPTOM–COMPLEX, WITH REPORT OF A CASE.[1]

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In 1893 Huchard proposed the name Adams-Stokes disease for a remarkable symptom-complex characterized by temporary or permanent bradycardia, loss of consciousness, together with apoplectic or epileptiform seizures. According to him the condition is usually if not exclusively encountered in individuals of advanced years, and is indicative of arteriosclerosis of the cardiobulbar type.

The first authentic case was reported by Adams in 1827, but those of Stokes, published in the early fifties, were better described and have been more frequently cited. A long interval elapsed before the observations of these earlier writers were accorded proper recognition, though other clinicians reported cases from time to time that were similar in every essential point. Among the more important contributions of this period are the papers of Cornil (1875) and Handfield Jones (1876). Both of these authors accurately outlined the peculiar symptom group and described cases that undoubtedly must be included in the same category with those of Adams and Stokes.

It was not until after Huchard had suggested a definite pathological basis for the complex that it was submitted to critical analysis, and some years passed before it was accepted as a distinct clinical entity. Case reports of more or less interest appeared in considerable numbers at this time, and we find casual mention of the condition in the text-books of Balfour (1894) and Edgren (1898). In 1899 a valuable paper was published by His in which he described for the first time clinically the unusual complication known as blocked heart or atrioventricular allorhythmia. In 1901 August Hoffmann considered the neuroses of the heart and bloodvessels of sufficient importance to justify separate consideration. His treatise on the subject was shortly followed by those of Cassirer and Ludwig Krehl. We are indebted to these authors for the systematic presentation of the neuroses of the heart, including the Adams-Stokes complex; however, it is necessary to supplement their statements by reference to the very able reports that have appeared since, especially those of Luce (1902), Jaquet (1902), Lewy (1902), and Osler (1903). A fair idea of the general literature of the subject may be obtained from the painstaking review recently compiled by Edes (1901).

[1] Read before the California Academy of Medicine, March 22, 1904.

It is proper to call attention at this point to the important services rendered in the development of functional heart diagnosis by von Basch, to whom we owe the sphygmomanometer. Mention should also be made of Schott, Gräupner, and of A. Smith, who have done much to perfect mechanical methods for the determination of the driving energy of the heart, and who have thereby aided materially in the investigation of the neuroses.

Etiology. A pulse rate under sixty is usually considered pathological, though Huchard states in his classification of the bradycardias that it is normally slow in some individuals. Napoleon is said to have had a pulse rate of 40, but there is reason to believe, from the statements of Corvisart, that he was subject at times to peculiar seizures which have never been fully described. Bradycardia may be induced experimentally by irritation of the pneumogastric nerve, compression of the carotids, or by a rise of arterial pressure. It may at times be observed after childbirth and during the period of convalescence from acute articular rheumatism and a number of the infections. Schuster (1896), for example, describes a case in a child of four after an attack of acute articular rheumatism, with a pulse rate varying from 35 to 130. The respiration was slow and irregular, and there were profuse sweats after each period of bradycardia. The case was probably one of acute myocarditis. Bradycardia may be caused by certain of the inorganic or organic poisons, and not infrequently is present in certain autointoxications, as, for example, in retention of bile salts without icterus (Brandenberg, 1903), and in the course of a number of morbid gastrointestinal hydrolyses. Slow pulse may occur in neurasthenia, hysteria, epilepsy, melancholia, amyotrophic lateral sclerosis, and tabes, but in none of these diverse conditions is the true clinical picture of the Adams-Stokes disease fully developed.

The Adams-Stokes complex most commonly occurs after middle life. It is rarely seen before the third decade. Of the twenty-five cases that I have analyzed, 76 per cent. were over fifty years of age. Males are more frequently affected than females, the ratio being nearly three to one. Syphilis may be a contributing factor, but was present in only two cases. Curtin (1903) has noted bradycardia with convulsions after excessive use of tobacco. Alcohol appears to have a definite causal relation. In a few instances a life of exposure seemed to predispose, but this factor cannot be emphasized. In the cases of Balfour and von Schrötter traumatism seemingly played a part. The typical complex may be associated occasionally with sclerosis of the bulbar vessels and attendant anæmia of the vagus centre, or parenchymatous changes may be found in the peripheral filaments of this nerve. Abortive forms are met with in individuals of neuropathic tendency. In this group belong the peculiar attacks of temporary bradycardia with dizziness, partial loss of consciousness, or of transient weakness of the extrem-

ities sometimes seen in neurasthenic or hysterical patients after periods of emotional excitement. These cases, as a rule, have a labile circulation and yield definite evidence of vasomotor instability.

Morbid Anatomy. The post-mortem findings are inconstant. Anatomical lesions of the heart and bloodvessels are relatively frequent. Artery degeneration may be widespread, but it is more common to find regional sclerosis. The fallacies that beset conclusions based upon macroscopic observation alone are clearly shown by the very thorough studies of Luce (1902). This author noted acute diffuse parenchymatous vagus neuritis with total disappearance of the axis-cylinder processes at many points, although at autopsy both vagi were regarded as normal, and nothing pathological was found in the medulla oblongata or the vagus centres. The arteries at the base of the brain sometimes present gross degenerative changes, but this is rather the exception than the rule. In the absence of accurate histological data, the greater part of the pathological reports at present available must be regarded with distrust. Undoubtedly in many instances essential changes in the peripheral vagi have been entirely overlooked.

Among the conditions affecting the heart itself those due to interference with its blood supply are most important. Sclerotic changes in the coronary vessels are frequently though by no means invariably present. Partial occlusion of one or both vessels may occur as the result of calcareous deposits at their points of origin. In one case, that of Sendler (1892), the vessel was partially occluded by the pressure of a primary fibroma of the heart.

In uncomplicated cases the heart is often not enlarged. Fragmentation of the muscle of the left ventricle has been reported, but in every instance must be regarded as an artefact. Fatty degeneration of the heart is not constantly present, as Friedreich thought, though it is common to find areas of fatty or fibrous myocarditis. The valves are often found intact in cases that had pronounced murmurs during life and gave every evidence clinically of extensive valvular disease. There may be imperfect alignment of the aortic segments, however, due to the presence of sclerotic nodules. In the remarkable case reported by Luce there was a primary round-celled sarcoma of the heart of the size of a hazelnut situated in the right ventricle, which partially invaded both the aortic and pulmonic orifices and gave rise to true bilateral obturating stenosis. As a rule there are no characteristic changes in the abdominal organs. The kidneys may be quite normal. Hoffmann (1901) quotes two cases of exceptional interest: that of Holberton, in which there were found narrowing of the occipital foramina, together with parenchymatous changes in the vagi and the superior cervical ganglion, and Lépine's case, due to compression of the pons and medulla.

Symptoms. Bradycardia, either permanent or recurrent, is always present, accompanied at irregular intervals by central nervous manifestations that are characteristic. The typical seizure may be preceded by a definite aura: sensations of weight and uneasiness in the epigastric region, or a sudden rush of blood to the head or extremities, are the more common. Stokes' patient was able to avert an impending attack by dropping on his hands and knees and holding his head down. Balfour mentions a parallel instance. His patient was able on one occasion to accomplish the same purpose while out walking by lying down in the road. In the fully developed attack there is sudden loss of consciousness lasting from a few seconds to hours, but usually of momentary duration. The patient falls; convulsive movements of the extremities ensue; the pupils are dilated; the respirations stertorous and at times of the Cheyne-Stokes type. The pulse rate is invariably diminished, and counts of 20 and under are not uncommon. In one case a rate of 5 was noted. There may even be gradual extinction of the radial pulse, with temporary cessation of heart action. In my case no pulse could be detected at the wrist during the attack. Various authorities claim to have heard indistinct tones or murmurs over the præcordia in the period of suspended activity. Hoffmann states that with the radiograph he was able to detect movements of the auricles while the ventricles were at rest. All attempts on my part to verify this observation were wholly fruitless owing to the impossibility of controlling the position of the patient during the convulsive phase.

The initial attack is usually of sudden onset and may affect an individual apparently in good health. In other instances there is an antecedent history of occasional dizzy spells extending over a considerable period. These prodromal attacks are, as a rule, of transitory nature and cause no particular inconvenience or apprehension. Once established, they tend to increase in frequency, though well-directed treatment will often give relief and even comparative immunity for some time. The attacks are subject to extraordinary variations both as regards frequency and severity. There may be several in the course of a day and then none for a week or more. Again, the seizures may be of hourly occurrence and lead rapidly to a fatal issue. I have frequently seen five or more in the course of an hour. His's patient had 143 in a single day. The exciting causes are indefinite, but it is certain that psychical factors play a much more important part than is generally stated. As a rule these patients are profoundly responsive to changes of environment, and under stress of emotional excitement may have frequently repeated seizures. In the milder attacks consciousness may be partially preserved and the patient able to maintain his balance by grasping near-by objects. In others loss of consciousness is absolute. Muscle movements set in, varying in intensity from

fibrillary twitchings to the most powerful convulsions, and the patient finally recovers consciousness to find himself in the prone position with no definite idea of what has happened. As a rule there are no serious after-effects, and the general health in the free period is unimpaired.

Evidence of vasomotor unrest is seldom lacking. Extreme pallor of the face, alternate blanching or reddening, coldness of the extremities, and drenching sweats after the attacks are the most common signs. It is difficult to escape the conviction that vasomotor disturbances initiate the attack in a large number of cases. Both Ortner (1903) and Jaquet emphasize this point. This is less true of those cases that exhibit permanent vagus overaction than of the larger group of recurrent bradycardias which usually are of labile type and frequently have pulse rates above normal in the interval between attacks. It is in this latter class that the vasomotor influence is the more marked.

Certain anomalies of the circulation are of special interest:

1. *Positive Centrifugal Pulsations of the Jugular Vein Exceeding in Frequency the Apex Beat.* This remarkable phenomenon, the clinical description of which we owe to His, appears to be due to auriculoventricular asynchronism or allorhythmia. As Sahli has pointed out, if we accept the evidence yielded by the experiment of Stannius, namely, that the idiomuscular movements of the heart arise in the auricle and are propagated thence to the ventricle, and that it is possible to produce dissociated movements by interrupting the path of the impulse at the auriculoventricular border, it follows that a lesion at this point may cause independent auricular contractions, with no accompanying movements of the ventricle. This affords a logical explanation of the venous pulse observed by His. His' patient had a radial pulse rate of 18 to 32 exactly isochronous with the apex beat, while the jugular pulse ranged from 96 to 104 and was isochronous, with a low, humming murmur heard to the right and left of the sternum in the second and third intercostal spaces. One of Stokes' patients (Edmund Butler) affords a parallel example, though the phenomenon was less well marked. Blocked heart must be regarded as of very grave import. According to Belski (1902) it is peculiar to the terminal period of various cardiopathies and indicative of a dying myocardium. For reasons that are sufficiently obvious, the venous pulsations observed in blocked heart may be confined to the bulbus jugularis.

2. *Heart Bigeminism or Pseudohemisystole.* Hoffmann observed this form of arrhythmia in a young woman who was subject to syncopal attacks and had a pulse rate varying between 18 and 30. According to Dehio it is possible to orient the causative lesion by the action of atropine. This drug will equalize the pulse rates at the heart and periphery if the vagus centre is involved, but not if the bigeminism is due to mural changes in the heart.

Special Physical Signs. 1. *Heart.* Inspection may reveal little of objective value. The rib cage usually is stiff and its range of movement restricted. There is no bulging in the precordial region. In a majority of patients the apex impulse is very faint or invisible and frequently cannot be detected in any position. As a rule it is within the nipple line.

Clinical and pathological reports concerning the size of the heart are not in harmony. Very commonly there is no demonstrable enlargement. Moderate hypertrophy of the left ventricle occurs in the cases of diffuse arteriosclerosis, and dilatation of the right ventricle usually takes place as a terminal event.

The heart sounds may be normal both at the apex and base. In some patients they are faint and distinguishable with difficulty; in others the tones are loud and ringing, with accentuation of the second aortic sound. Murmurs are relatively frequent. A soft blowing systolic murmur at the apex is the most common, but occasionally loud systolic murmurs are heard at every orifice, and it is astonishing over what a large area these sounds may be audible. Coincident pulmonary stiffness and distention, to which von Basch and, later, Zuelzer (1901) called attention, may facilitate the diffusion of the sounds by offering a better vibratory medium. Alien tones of doubtful genesis occasionally invade the heart cycle. They are usually low and indistinct and arise in the interval between the first and second sounds. It is necessary to exclude heart bigeminism. Very rarely low humming sounds may develop at the base; their significance has already been discussed in connection with heart block.

2. *Arteries, Blood, and Blood Pressure.* The peripheral arteries are often stiff and tortuous. This is especially true of the temporals, which may be very rigid and prominent. Arterial degeneration is not invariably present, however, as a large number of patients appear to have vessel tissue of good quality.

So far as I am aware the blood characters have never been worked out. Hoffmann's patient had 55 per cent. of hæmoglobin. Lewy states that he was unable to count the cells, as every attempt to withdraw a specimen precipitated an attack.

Huchard thinks that the blood pressure is high during the attack. No definite statements occur in the literature.

3. *Urine.* Hoffmann states that the secretion of urine is diminished before an attack, but admits that the evidence is not conclusive. In a large majority of patients it is of rather low specific gravity, free from albumin and sugar, and relatively negative.

Course and Prognosis. The outlook will depend largely upon the age and causative lesion. When the complex develops after middle life as a functional disorder in the absence of organic heart disease, the prognosis is favorable as regards life and the condition may be well borne for years. The outlook is, as a rule,

favorable also in the abortive forms occurring in young individuals as the result of blood changes and psychical disturbances. Even in cases of more severe type the attacks may be withstood for ten years or more. Marked irregularity of the pulse, heart block, and other evidence of myocardial involvement are of the gravest import and may rapidly lead to a fatal issue. Death usually occurs in an attack.

TREATMENT. All attempts to cut short the characteristic attacks have so far been unsuccessful. Rest in bed should be enforced in all cases where the seizures are of daily occurrence. The foot of the bed should be elevated. Visitors, particularly those nearly related, should be excluded and every possible step taken to insure both mental and physical quiet. The diet should be simple and easily digestible. Tea, coffee, and tobacco must be absolutely prohibited.

Internal treatment is on the whole unsatisfactory. Potassium iodide in small doses—ten to twenty grains per day—is the most generally applicable remedy, and it may be given with benefit for long periods. Inhalation of oxygen is recommended by Hoffmann. Twenty-five to thirty litres may be taken daily for several months. The bromides are seldom of service. Digitalis is of doubtful value and must be used with extreme caution.

Residence in an equable climate is advantageous and should be recommended, together with instructions as to the avoidance of worry and physical exertion.

The pathological physiology of the Adams–Stokes complex is obscure. Of necessity it must remain a source of speculation until the causative factors are better understood. Taking into consideration the fact that a majority of all cases concern patients past middle life, and that it is customary to assume circumscribed or diffuse artery stiffness as an essential condition, it is natural to suppose that blood pressure studies would be instructive. On this important point, however, there are no authoritative statements in the literature.

The case I am about to present has been under observation nearly two years. During this period the object has been to accumulate trustworthy data on blood-pressure variations by making frequently repeated determinations. It will be necessary, therefore, to briefly describe the apparatus employed and the method of investigation, before proceeding with the clinical history of the patient.

All blood-pressure measurements were made with an improved form of the Riva-Rocci sphygmomanometer. This instrument is now so widely known that it will be unnecessary to describe it in detail. The apparatus is designed to register in millimetres of mercury the air pressure required to obliterate the pulse wave in the brachial artery. The arm band most commonly used in this country is about 5 cm. in width, made of thin rubber protected by a

jacket of canvas or duck, and is not provided with a rigid outer shell to prevent unequal distention. Müller (1902) in a simple theoretical discussion, made clear the inherent defect of this arm band and called attention to the fact that with it the normal values obtained are too high, ranging between 140 and 150 mm. He adopted in preference one designed by von Recklinghausen, which is less open to objection. This form consists essentially of a thin rubber cylinder 15 cm. in diameter, coated on the outer side with thin silk and applied around the upper arm by means of an ingenious double clamp. A strip of thin sheet brass of equal width is fitted smoothly over this and prevents unequal distention. With this band Müller obtained normal values varying from 105 to 115 mm. A similar band made for me by Zimmerman, of Leipzig, was used in all blood-pressure determinations carried out in the course of this investigation.

Observations were made, as a rule, with the patient in a sitting position. The band was first applied to the bared arm at the level of the heart, and the patient instructed to assume an unconstrained attitude. After from fifteen minutes to half an hour of rest, pressure observations were made in triplicate. Readings were taken under three sets of experimental conditions: 1. At once after walking ten blocks at a slight up grade, omitting the fifteen-minute period of rest. 2. After rest for at least a quarter of an hour in a comfortable position. 3. Immediately after taking a prescribed amount of active exercise—walking and running in a room three minutes with no period of rest. No difficulty was experienced in obtaining concordant readings, the maximum variation never exceeding 2 mm. Muscle movements of any sort introduce a gross error. For this reason it is impossible to determine blood pressure during typical convulsions.

Pulse tracings were taken with the ordinary Dudgeon sphygmograph. Unfortunately means were not at hand to determine the relation of the pulse curve to the respiratory cycle. A graphic presentation of the results, together with the conclusions deduced therefrom, will be introduced after reviewing the clinical history of the patient.

E. L., aged seventy-two years, a baker by occupation, applied for treatment at the Medical Dispensary of the University of California about June 5, 1902. He stated that the first symptoms of his trouble made their appearance in February of the same year. At that time he was working at his trade in a country town and was required to report for duty during the night. The actual onset was preceded for some days by indefinite symptoms. He was nervous, depressed, and had to urinate with unusual frequency during the day and four or five times at night. While on his way to work one evening he read a letter containing bad news; had what he describes as a rush of blood to the head, and fell unconscious to the ground.

The attack quickly passed off, however, with no unpleasant after-effects, and did not prevent him from engaging in his usual duties. Later in the evening, while stooping over the oven, an abortive attack was experienced, with a partial loss of consciousness and a feeling of suffocation and distress. Toward morning he again fell in a syncopal attack, but soon regained consciousness and was able to walk home. From this time on the seizures were of daily occurrence, forcing him within a short time to give up his work. A period of rest proved beneficial, but the trouble reappeared in May and induced him to consult a physician. The results of treatment were unsatisfactory. Indeed, under the influence of digitalis, which had been ordered for him, the attacks recurred with greater frequency, until finally, becoming alarmed about his condition, he moved to the city.

The following notes were taken at the medical clinic:

The patient was the youngest child in a family of nine. Both parents died at an advanced age. The father had been a hard drinker for years, but always enjoyed good health.

Patient was a delicate child. In his seventh year an ulcer developed on the posterior surface of the middle third of the right thigh, remained open several years, and from time to time discharged pieces of bone. Under treatment it gradually closed, but he was compelled to get about on crutches for several years. In his eighteenth year he had pleurisy, does not remember which side was affected, but declares that the condition recurred once a year for seven years. It finally disappeared after a severe illness suggestive of typhoid fever, which occurred in his twenty-fifth year. After this for a considerable period he enjoyed good health, except when under the influence of whiskey, which he has used to excess since his thirtieth year. At the age of forty-eight a painless swelling developed on the dorsum of the right hand. It proved of transitory nature, but has frequently recurred. There is no definite history of rheumatism, except that at times he has had some stiffness of the right hip and knee. In his sixtieth and again in his sixty-second year he had severe attacks of pneumonia. During the past nine years his health has been good, and he has worked steadily at his trade. He positively denies any venereal infection.

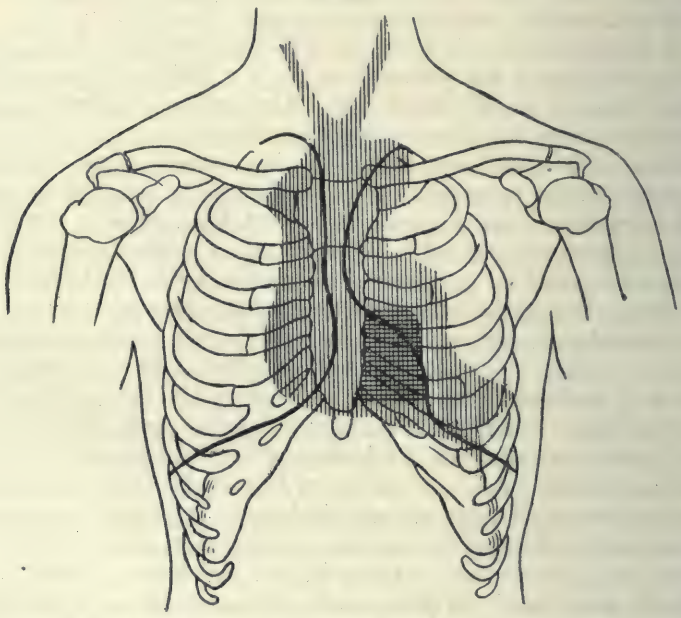
Examination. Short, slightly stooped man of moderate musculature, fairly well nourished. The skin is soft and of good color; a few purpuric spots are present on the upper arms and shoulders; there is slight dermographia. The facial expression is dull. The lower eyelids are baggy. The pupils are rather large, equal, and react briskly to light and accommodation. There is a well-marked arcus. The ears are negative. The tongue is clean, the palate well arched, and the throat free of abnormalities. The teeth are bad. The mucous membranes where visible are of good color.

The thorax is symmetrically developed and roomy, though stiff

and of limited mobility, the free costal borders slightly everted, the xiphoid angle wide. The apex impulse is neither visible nor palpable. On percussion the base of the heart is at the third cartilage, the apex half an inch inside the nipple line in the fifth interspace. The right border of dulness is at the left border of the sternum; the left border is 7½ cm. from the median line.

At the apex there is a musical systolic murmur, faintly heard also in the midaxilla, but inaudible at the point of the scapula. It is clearly heard at the junction of the eighth rib with the anterior axillary line. In the second right interspace there is a musical systolic murmur which can be clearly heard in the right carotid

Fig. 1.



artery, less clearly in the left. The tone qualities of this murmur exactly coincide with that heard at the apex. The most painstaking examination failed to reveal convincing evidence of multiple valve lesions. Starting from a point of maximum intensity midway between the apex and aortic region, the murmur can be traced over a wide area corresponding roughly to an outline including the heart and arch of the aorta, with a margin about three inches wide (see Fig. 1). The basic tones are clear, and there is no duplication. The second aortic sound is slightly accentuated. The tricuspid region is negative. There are no pulsations in the veins of the neck.

The radial and femoral arteries are neither hard nor tortuous, while the temporals, on the contrary, are rigid and prominent. The

pulse rate in the radial artery is 40, corresponding exactly to the apex beat. The pulse is occasionally intermittent.

The blood contains 10,000 leukocytes, 5,790,000 erythrocytes, and 88 per cent. of hæmoglobin. A second leukocyte count several days later gave 6600 cells.

The breath sounds are clear and very harsh, inspiration is somewhat prolonged, and there is slight dyspnœa on exertion.

The abdomen is flat, with no inequalities, and the reflexes are intact. There are no sensitive points. The liver is not enlarged; its lower border is smooth and barely palpable. The spleen is negative. The kidneys cannot be felt. The urine is clear, of light-amber color, sharply acid, and a normal mucous cloud separates on standing. The specific gravity is 1020. There is a faint trace of albumin, but no sugar. In the sediment there are large numbers of barrel-shaped crystals of uric acid. There is very little epithelium, not more than represents the normal desquamation from the bladder wall. A few unaltered red blood cells are present, but no pus. There are a few hyaline and finely granular casts.

The left thigh is smaller than the right and shows a linear, deeply depressed scar in the middle third posteriorly. In both legs below the knees there are a few small varicose veins, but no œdema.

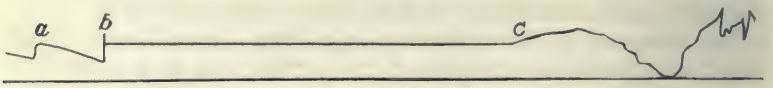
There are no disorders of sensation: heat, cold, and pain reactions are intact. The knee jerks are lively, the left more pronounced than the right. The cremasteric reflex is present, but very sluggish.

He is positive that his trouble has been greatly aggravated by the action of digitalis, which he has been taking for some weeks. When he first came under observation he had many attacks daily. It was not uncommon to count ten or more in an hour. At times the slightest disturbance—speaking harshly, or slamming a door—would precipitate a seizure. Raising the extended arm over the head was for a considerable time a certain provocative measure. He is able to predict the moment of onset by a sensation of blood rushing to the head, and at once adopts an attitude of absolute immobility. In the attack the head is held well down between the shoulders; the chin thrust forward; the eyes wide open, with dilated pupils; the expression very anxious. A chair or other support is suddenly grasped; consciousness is suspended; the respiration becomes stertorous; the body is bent forward on the hips; the arms and legs partly flexed and very rigid. This tonic condition is succeeded by irregular clonic contractions, which affect both extremities simultaneously, but quickly pass off, the whole attack lasting from five to fifteen seconds. The skin is moist with perspiration after the seizure.

The behavior of the pulse is characteristic. By careful palpation it is often possible to detect an oncoming attack. The pulse waves become less frequent, dropping from 40 to 26 or less, with perhaps slight arrhythmia, then fade out entirely, and the heart ceases to

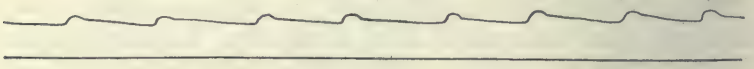
beat. By consulting Fig. 2 it will be seen that absolute heart rest occurs some time before the convulsive phase, since the slightest movement of the wrist tendons suffices to disturb the tracing device. At *c*, Fig. 2, the beginning of the muscle tremor is plainly indicated.

FIG. 2.



In order to obtain a tracing characteristic of the period of heart rest, it was necessary to apply the sphygmograph, await an attack, and then liberate the recording mechanism at the moment of heart rest. Unfortunately this gives no clue to the pulse characters before the onset. The sphygmograms taken in the free period vary very little in their general form. The tracing shown in Fig. 3 illustrates the

FIG. 3.



essential features, especially the gradual decline, with no dicrotism. The period of heart immobility does not terminate at the beginning of muscle movements; on the contrary, it persists throughout the attack. No sound could be heard over the præcordia at this time. Repeated attempts were made with the radiograph to investigate the heart movements during a seizure. Little of value was noted, however, owing to the suddenness of onset, brief duration, and the violent movements of the body.

A simple dietary, mostly liquid, was ordered, the tincture of digitalis withdrawn, and small doses of nitroglycerin substituted. After a week, no definite improvement being noted, the nitroglycerin was replaced by potassium iodide, five drops of the saturated solution three times daily. Within a short time marked improvement became apparent. The pulse, which previously had ranged between 30 and 40 in the free period, now rose to 72. The syncopal attacks became less frequent, and toward the end of July entirely ceased. The patient was dismissed from the clinic at his own request.

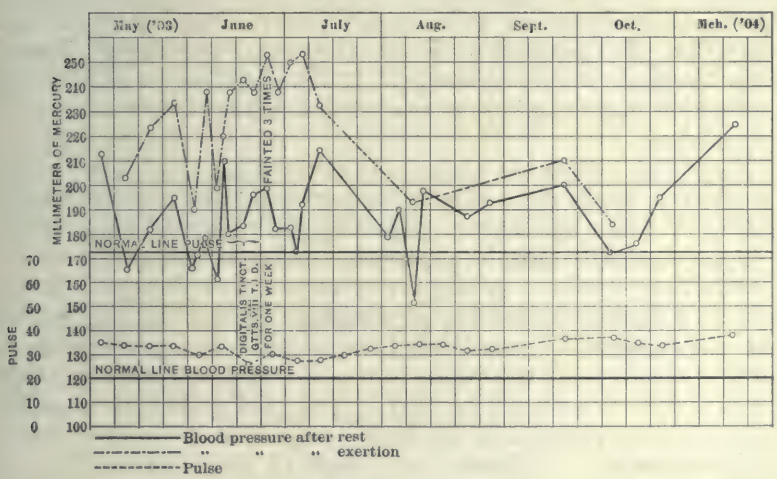
On October 11, 1902, he again applied for treatment, having had several dizzy spells during the past week. Reports that he stopped taking the iodide solution shortly after leaving the clinic. During September he had fair health, but latterly has been "seeing black." A physician who attended him recently ordered digitalis and nitroglycerin. Three days thereafter the typical seizures reappeared. He had two attacks while undergoing examination, which were rather less severe than those previously seen. At the wrist the

pulse rate was 62, quite regular, corresponding exactly to the apex beat. The heart condition was unchanged. The urine was intensely acid and contained large numbers of uric acid crystals. The amount in twenty-four hours was 1575 c.c., with a specific gravity of 1018. Between the 11th and the 23d of October he took twenty drops of saturated solution of potassium iodide every day. The pulse rate averaged 72; the subjective condition was good and he had no attacks.

On May 21, 1903, he reported that he had had no fainting spells since October. At times, especially in foggy weather, he has had some dizziness, but in other respects he has been quite well. There was no change in the heart condition. The pulse for some time had been very slow, rarely exceeding 40; on that date it was 36.

On March 7, 1904, the subjective status was excellent. He had been taking the iodide solution continuously since October, 1902. Occasionally, especially in foggy weather, he had spells of "seeing black." He stated that the condition sometimes persisted for a minute or more. There were no new objective signs. The heart was unchanged. The murmur had the same distribution and characteristics last reported. The pulse was 38 and regular. The skin was soft, clear, and of remarkably good color. The urine contained a trace of albumin, was intensely acid, contained large numbers of uric acid crystals, and its specific gravity was 1020. A few hyaline casts were found.

FIG. 4.



The blood-pressure observations were begun May 21, 1903, nearly a year after the patient was first seen, and some time after the last series of severe attacks. A graphic presentation of the results is given in Fig. 4.

The following general conclusions are drawn from the experimental data obtained:

1. The blood pressure is constantly very high, ranging from 170 to 250 mm.

2. The great arterial trunks of the extremities are fairly elastic.

3. Although very high blood pressure has existed for at least a year, the urine is normal in volume and specific gravity; there is little evidence of diffuse interstitial nephritis or of left ventricular hypertrophy. From this it follows that the high pressure is well borne by the heart and kidneys.

4. Active exercise, as a rule, has no accelerating action on the pulse. I have never counted an increase greater than two waves per minute. On the other hand it occasionally exaggerates the bradycardia.

5. Exercise invariably causes a sharp rise of pressure.

It seems difficult to harmonize such contradictory findings with the prevailing theory of the circulation. It will be sufficient to emphasize the most conspicuous anomaly, namely, the manifest disparity between the laggard work of the heart and the tremendous pressure at the periphery. This would appear to be too great to permit of explanation by a theory which assigns to the left ventricle almost the entire work of overcoming the inertia of the blood column. In the light of recent knowledge there is reason to believe that the arterial system and the vast capillary network of the periphery constitute a powerful secondary mechanism in constant rhythmic activity. It will be apparent that such a supposition denies that the heart wall generates the entire motive power, assuming on the contrary that other portions of the blood vascular system contribute a large quota of the driving energy. It is well to bear in mind in this connection that the whole arterial structure has perfect anatomical continuity.

Hasebroek (1903) has attempted to establish a new theory of the circulation, which gives this secondary apparatus a more definite value. Whether his dictum regarding the motor function of the peripheral vessels may be accepted is open to debate. There is confirmatory evidence in support of such a view, however, and it affords a logical explanation of a number of vascular phenomena that are otherwise almost wholly inexplicable. It would be entirely beyond the scope of this paper to consider in detail the arguments for and against such a view, but it is my belief that the so-called Adams-Stokes phenomena are highly suggestive of the existence of such an auxiliary mechanism dominated by the vasomotor system. The mode of action of psychic and other stimuli which are able to produce unstable equilibrium of this balanced heart and peripheral machine remains doubtful, but it is safe to assume that in the future this problem is destined to occupy a much more conspicuous place in the annals of research.

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BORATED FOOD AS A CAUSE OF LESIONS OF THE KIDNEYS.

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Of the various chemical preservatives of food, the two most commonly employed are borax and boric acid, and these are used very largely together. They are used so extensively that it is safe to say that not only in the cities and large towns where the commercial importance of chemical preservatives is so great, but in the country at large, persons of all ages are likely to receive frequent, if not daily, doses of one or of the other or of both. They are added to milk, butter, oleomargarine, and some forms of cheese; they are almost always present in opened clams and oysters; they are applied externally to fresh meats to prevent sliminess and to fresh and salted fish; they are important constituents of the brine in which meats are pickled and corned; their solutions are injected into hams and other pork products, and they are to be found in almost every known make of sausages in the market, even those which are put up in hermetically sealed cans. It is commonly and correctly supposed that canned foods, having been subjected to the process of sterilization, need no chemical preservative; but these agents are used in canned sausages, not to prevent decomposition, but because they increase the water-retaining capacity and prevent the sausage contents from contracting and thus causing the casing to appear loose and wrinkled.

As much as 0.87 per cent. of boric acid has been found by Popp and Fresenius[1] in canned sausage, and even 2.8 per cent. by Kister[2] in canned crab meat. American corned beef has been known to contain 3.87 per cent., and pork (see instance below) kept three weeks in borax has yielded 4.05 per cent., its innermost parts containing as much as 2.73 per cent. Polenske[3] found borax in every one of fifty-one specimens of American preserved meats, the majority of which contained more than 1 per cent. Thus, nineteen contained between 1 and 2 per cent.; thirteen from 2 to 3 per cent., and one as much as 3.36 per cent. Here again the boron compounds are used not wholly on account of their preservative influence, but because they do not withdraw water as salt does, and hence the meat tends less to become tough and stringy. Moreover, they preserve the natural color, while salt destroys it. It has been said, in answer to objections made by the German Government and others to the use of borax as an external application and as a constituent of pickling-brines, that that which adheres to the surface is easily washed away and that that which penetrates the tissues is removable by soaking. This, however, is not true. Once established in the tissues, it cannot be soaked out, nor even boiled out. Heinze[4] soaked for twelve hours a piece of meat containing 1.16 per cent. of boric acid, and found that even then it contained 0.93 per cent.; and Beythien and Hempel[5] washed a piece containing 1.12 per cent. for twelve hours in running water, and then recovered 0.69 per cent. Polenske[6] examined a 600-gram piece of fresh ham that had been kept three weeks in powdered borax, and found in the outer fat, 0.076 per cent.; in a piece cut from the middle, 2.73 per cent., and in a fair sample of the whole, 4.05 per cent. Two fresh hams, weighing twelve pounds each, were kept, one in boric acid and the other in borax, for four weeks; then they were washed, and from each was taken for chemical examination a slice 10 x 6 x 6 cm. It was found that into each one the chemical had penetrated very thoroughly, so that one may not say in a given instance whether the drug soaked in or was injected.

In milk the addition of from 0.1 to 0.2 per cent. of a mixture of the two is recommended, an amount which seems insignificant until we observe that it is equivalent to from 15 to 30 grains per quart. It is asserted that its presence in butter to the extent of 35 grains to the pound is necessary and harmless, and in several countries this admixture has received official sanction. With curious inconsistency, not one, but several, government commissions

[1] Zeitschrift f. Offentliche Chemie, 1897, p. 155.
[2] Zeitschrift f. Hygiene u. Infectionskrankheiten, 1901, Bd. xxxvii. p. 226.
[3] Arbeiten aus dem Kaiserlichen Gesundheitsamte, 1900, Bd. xvii. p. 561.
[4] Chemiker Zeitung, 1899.
[5] Zeitschrift f. Untersuchung der Nahrungs- u. Genussmittel, 1899, p. 842.
[6] Arbeiten aus dem Kaiserlichen Gesundheitsamte, Bd. 1902, xix. p. 167.

have decided that, although borax and boric acid are highly objectionable in milk, their presence in butter and concentrated milk to the extent of 35 grains per pound and in cream to the extent of 17.5 grains per pint is a commercial necessity of no sanitary significance. To clams and oysters opened at the place of taking and shipped in bulk to distant points, they are added with a generous hand. I have seen no reports of analyses, but I have found as much as 4.5 grams (reckoned as boric acid) in a pint of Norfolk oysters bought in Boston.

Concerning the preservative power of the boron compounds there is some dispute, but the fact remains that, for general purposes, they meet the requirements of trade better than any known substance. It is true that food already undergoing decomposition cannot be made sound, and that the process of putrefaction, once started, cannot be checked by either boric acid or borax; but it is equally true that, even though they do not kill bacteria, they inhibit their growth. Infected meat treated with these substances will keep much longer than if untreated, and, indeed, without losing its capacity for producing injury. Thus, von Fodor killed an animal twenty-four hours after it had been inoculated with anthrax, and treated a part of the meat with borax. After a number of days, the untreated portions became putrid, but the borated meat appeared to be normal in all particulars, although it was swarming with anthrax organisms.

When added to milk to the extent of 1 to 2 grams per litre (0.1 to 0.2 per cent.), it has no very great influence in postponing souring, although with proper precautions, in themselves influential, coagulation may be deferred as long as three days; but under ordinary conditions the accomplishment of this result would require the presence of so much of the preservative as to destroy the natural taste.

Whether or not the boron compounds are capable of causing injury to the consumer of borated foods, has been the subject of much experimentation and heated controversy. Reviewing the literature, one is struck at once by the fact that adverse opinions are based largely upon occasional untoward results of boron medication, upon feeding experiments extending over but a few days, and upon *a priori* reasoning, and that favorable reports are based upon equally insecure foundations. A very large part of the experimental work has been limited to the determination of their action upon digestion and metabolism, and most of the researches have been of very short duration. Many of those interested on both sides of the question have been content to make a few observations, and then have dismissed the subject with a wave of the hand as settled for good.

It is not to be supposed that any food preservative that will produce obvious injury within a few days or weeks can ever come into

general use; and an experiment lasting but a few days and involving the introduction into the system of but a few grams of a chemical not classifiable as a poison can have no probative force. For example, an experiment much quoted by the opponents of boron and fiercely assailed by its friends is that of Kister,[1] who gave 3 grams of boric acid daily to three men, one of whom was made sick at once with vomiting and diarrhœa, and withdrew; a second had albuminuria on the fourth day, when the administration of the drug was discontinued and the albuminuria disappeared; and the third lost his appetite on the seventh day, had albuminuria on the tenth, ceased to take the drug on the twelfth, and became normal on the thirteenth.

Neither of the subjects whose service lasted beyond the first day was given more of the drug to ascertain if a causal relation existed between it and the albuminuria, which may have been an incident of any one of a number of conditions. Another, ascertaining that a food of somewhat complex composition (blanc mange) was made partly with milk which contained borax, attributed the sickness of a number of persons who ate of it, and the death of some fowls that consumed the remainder, to the toxic nature of borax, without considering other possibilities or trying the effect of borax alone on other fowls. Others, reviewing the literature, have brought together the various effects that have been observed in subjects of experiments and in patients with idiosyncratic tendencies, and have proceeded to draw unjustifiable conclusions. Thus, one insists that the results of eating borated foods are vomiting, diarrhœa, diuresis, lesions of the skin, interference with absorption of food, excretion of abnormally large amounts of nitrogen, and loss of weight.

It is well known that certain individuals cannot undergo borax or boric acid medication any better than certain others can take quinine or morphine, or eat lobster and strawberries; and when we read, as we may in recent medical literature, of ill-effects from the use of a 2 per cent. solution of boric acid as a mouth-wash, of skin eruptions following repeated washing of the bladder with boric solution; of nausea, loss of appetite, and depression following the dressing of open wounds with boric ointment; of total baldness following internal administration of 10 to 20 grains daily for five weeks, and of death from washing out a stomach with a 2.5 per cent. solution, we recognize that these must be isolated cases of idiosyncratic susceptibility from which it would be highly unscientific to generalize. It is often charged that borax and boric acid cause diarrhœa, but such a statement deserves but little consideration. It may occasionally happen in experiments that the subject is purged, but it must be remembered that in the present

[1] Zeitschrift f. Hygiene u. Infectionskrankheiten, Bd. xxxvii. p. 225.

state of the food supply one is likely any day to swallow more or less of both with fish, oysters, ham, corned beef, sausage, milk, and butter, and yet we are not continually purged. Indeed, those who are chronically constipated doubtless absorb borates frequently without relief.

On the other hand, experiments of short duration yielding no evidence of injury to digestion have been accepted as demonstrating the absolute innocuousness of the boron compounds as food preservatives, regardless of the fact that they prove little or nothing as to possible effects of long-continued ingestion on the different organs of the body. It is true that, so far as they go, the weight of evidence of digestion and metabolism experiments is slightly in favor of the defendant substances; but such experiments, as a rule, are not carried far enough. Concerning the value of short researches of this character Liebreich,[1] who is doubtless the most strenuous advocate of the use of the boron compounds in foods, says: "It must always be emphasized that no absolute conclusions are admissible after a single series of experiments of such short duration, particularly with experiments on metabolism, which in themselves call for strict criticism, especially in the case of human beings."

As has been stated above, no substance capable of inducing acute symptoms of any kind could long be employed as a food preservative. The use of a substance, for example, which would cause nausea and vomiting, or diarrhœa, or headache, or eruptions of the skin, or other symptoms, which, occurring in large numbers of people at the same time, would direct attention to the food supply, would necessarily be of short duration. With such as cause no such effects, it is manifestly absurd to institute short researches with any expectation of positive results. The preservatives in common use are either harmless or they produce injury insidiously on long-continued ingestion; and in the latter case it is not to be expected that every individual subjected to their influence will be affected to the same extent.

Owing to the fact that one cannot possibly have a record of the nature and amounts of the various substances that for weeks and months and years have been taken into the system, and that the influence of this and that condition to which one has been subjected cannot be measured, it is not possible in case of discovery of the existence of pathological processes definitely to trace the cause thereof back to food. Let us suppose, for example, that A. B., after some weeks of not feeling well, consults his physician and undergoes a thorough examination, in the course of which are found albuminuria and other evidence of degeneration of the kidneys. Is it likely that his condition will be attributed to the character of

[1] Second Treatise on the Effects of Borax and Boric Acid on the Human System, London, J. & A. Churchill, 1902.

his food? And even if it were, would it be possible, in the absence of samples of everything that he has eaten for a long time, to single out the particular components of his diet which, nowadays, is likely to contain so many representatives of the pharmacopœia? Manifestly not.

In all that has been published concerning the influence of borax on the system, the most striking facts have come not from metabolism experiments, but from its therapeutic use. It has repeatedly been shown, notably by Dr. Féré, that the medicinal use of borax is not unattended with risk of producing or aggravating lesions of the kidneys. Liebreich,[1] however, stated in his first communication concerning the effects of boron compounds on the human system that weak and diseased kidneys bear borax and boric acid particularly well. In his "Second Treatise," he relates that to each of eight rabbits a single intravenous dose of borax was given without producing any evidence of renal irritation, and he says, therefore, in heavy type: "From these experiments on animals it may be deduced that borax is entirely innocuous as regards the functions of the kidneys." He gave boric acid to seven patients in varying amounts and for different periods. Two received 28 grams in seven days; three received 33 grams in eleven days; one took 37.5 grams in twenty-two days, and another 39.9 grams in twenty-four days. Daily examination of the urine revealed no albumin. To five others he gave borax in smaller doses (14.1 grams in twenty-six days, 38.7 in thirty-two days, 60.9 in thirty-seven days, 24 in fourteen days, and 23 in fourteen days). In two of these patients, slight temporary albuminuria was observed. To another man he gave 3 grams of borax on each of three days about two weeks apart (November 8th and 22d and December 2d). Examination of the urine on November 19th and 27th and December 8th showed no albumin. From the results observed in these three brief experiments he says, quite unmindful of his above-quoted statement concerning absolute conclusions from single series of experiments: "The above-named investigations offer a further proof that borax and boric acid are substances which cause no injury to health when judiciously used." Without further discussion of the clinical evidence of the possibility that the boron compounds may injuriously affect the kidneys, I will submit the details and results of a feeding experiment which I have lately conducted for a period of nineteen weeks.

Twelve healthy male cats were selected and kept under precisely the same conditions in separate cages. All were fed on the same food with this difference: One (No. 1) received no preservatives; six (Nos. 2, 3, 4, 5, 6, and 7) received borax to the extent stated below, and the remaining five (Nos. 8, 9, 10, 11, and 12) received

[1] Vierteljahrsschrift f. gerichtliche Medicin, 1900, p. 83.

another preservative which proved to be innocuous. The cats that were fed on borated food received the following amounts of borax:

No. 2	. . . . .	72.5 grams	in 133 days.	Average dose	0.544
" 3	. . . . .	112.0 "	133 "	" "	0.842
" 4	. . . . .	28.0 "	42 "	" "	0.667
" 5	. . . . .	108.0 "	133 "	" "	0.812
" 6	. . . . .	106.5 "	133 "	" "	0.800
" 7	. . . . .	48.0 "	56 "	" "	0.857

Of the dozen animals under observation, but three showed any sign of illness, and they were of the borax group. No. 4 sickened very soon, and died at the end of the sixth week; the other two were sick occasionally, but during the last weeks of the experiment they appeared to be normally active. Each subject was weighed at the end of each week; all showed occasional losses, but with the exception of No. 4 there was a net gain ranging from 230 to 990 grams.

At the expiration of the periods above mentioned, all of the animals were killed (No. 4 died as stated), and in each case the heart, lungs, liver, spleen, kidneys, lymph nodes, bone-marrow, pancreas, thyroid, thymus, adrenal, large bloodvessels, striated muscle, stomach, and small intestine were examined microscopically by Dr. E. E. Tyzzer, of the Department of Pathology.

The control cat (No. 1) showed no lesions whatever. Cat No. 2 showed a slight cirrhosis of the liver and nothing more.

Cat No. 3 showed kidney lesions, described below, and a slight increase of fat at the periphery of the lobules of the liver.

Cat No. 4 showed kidney lesions, described below, a small contracted spleen, slight increase in connective tissue in the liver, multiple adenoma of the pancreas. The lymph node showed increased fibrous tissue and was filled with epithelioid cells.

Cat No. 5 showed kidney lesions, described below, and fatty, but not markedly, degenerated liver.

Cats Nos. 6 and 7 showed kidney lesions, described below, and minute foci of lymphoid cells in the liver, generally peripheral to the lobule.

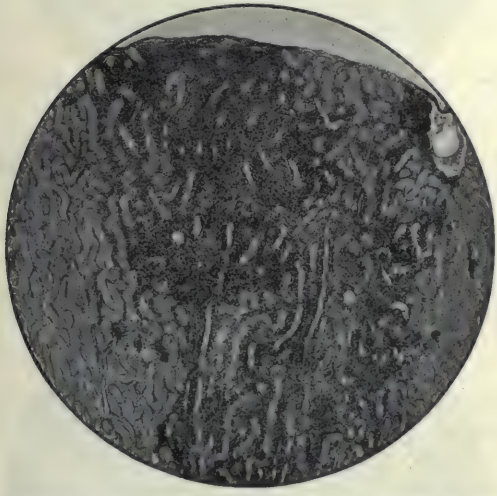
Cats Nos. 8 to 12 inclusive, which were given another preservative, showed no marked changes in the kidneys and no important or constant lesions elsewhere. Except that so far as the kidneys are concerned they may be regarded in the light of additional controls, they have no place in the present paper.

Thus, of the twelve cats, only five showed any marked changes in the kidneys, and these were all members of the borax group, only one (No. 2) of which escaped. The fact that five of this group, and none other, showed marked changes in the kidneys is significant; it cannot be looked upon as a matter of mere coincidence.

The stained sections of the five kidneys were submitted to Professor William T. Councilman, who very kindly reported thereon as follows:

"Five kidneys. All show lesions of the same general character, but differing in intensity. They consist, first, in degeneration of epithelium in all tubules, but most marked in the convoluted tubules. The normal fat vacuolation is very greatly increased, and in addition there is swelling and, in places, disintegration of epithelial cells, with fragmentation of nuclei. In the lumen of many of the collecting tubules are round and irregular granular masses representing cell fragments coming from higher up. Tubules also are found almost completely stripped of epithelium. In one kidney the change is entirely confined to degeneration of intense character, with hyaline casts in the small tubules. In the other cases the degeneration is not so intense, but is accompanied by foci of cellular infiltration. The largest of these foci is 2.5 by 3 mm. The infiltration is chiefly marked at the cortex and also around single glomeruli. Where this

FIG. 1.



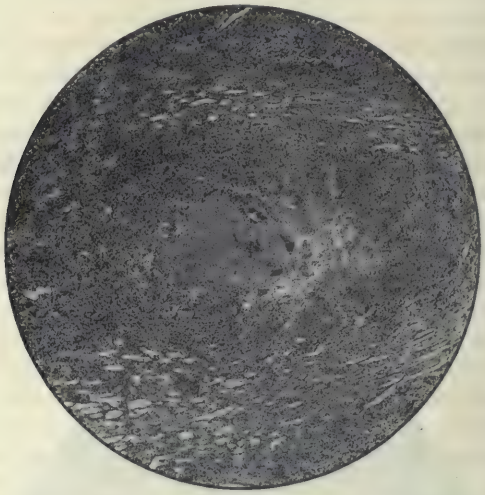
Foci of intense interstitial infiltration at the cortex, with degeneration and destruction of tubules. (15 diameters.)

is most intense, the tubules are entirely destroyed. In one large area in the pyramid there is circumscribed necrosis with invasion of phagocytic cells. These lesions are analogous to those found in subacute and chronic nephritis in man, although they do not conform to any definite type."

It may be objected that the daily doses of borax given were very large and, in proportion to weight, much greater than a person could possibly receive in food in the course of a day, but that is not so, and, moreover, it must be remembered that this substance is asserted to be absolutely innocuous even in large doses, and, indeed, rather beneficial than otherwise. Thus, it is said that for years Virchow took a daily dose of a gram, and

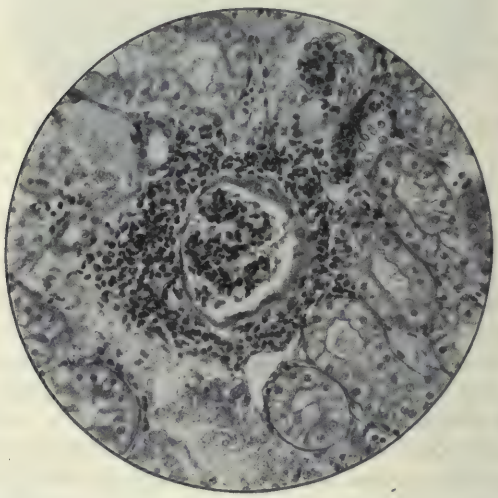
in the last years of his life 2 grams with benefit, though in what manner is not stated. But one can easily swallow, without know-

FIG. 2.



Focus of cellular infiltration in pyramids, with complete necrosis of tubules and invasion of phagocytic cells. (15 diameters.)

FIG. 3.



Focus of cellular infiltration around glomerulus, with degeneration and hemorrhage in adjacent tubules. (100 diameters.)

ing it, very much larger amounts in a day, and even with a single meal. We have, for example, the following known possi-

bilities: milk, 2 grams per quart; butter, 2 grams per pound; cream, 1 gram per pint; oysters, 4.5 grams per pint; corned beef, 18 grams per pound; ham, 18 grams per pound; sausages, 4 grams per pound. An oyster stew made with a pint of such milk and a quarter of a pint of such oysters, followed by a quarter of a pound of such ham or corned beef, would constitute a not extraordinarily hearty meal for an average man, who would ingest therewith upward of 7 grams of borax and boric acid, an amount which in the course of a day's food might easily be doubled.

INHALATION OF GASOLENE VAPORS.

By Torald Sollmann, M.D.,
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(From the Pharmacological Laboratory of Western Reserve Medical College, Cleveland, Ohio.)

Some years ago (1897) I began an investigation of the effects of gasolene vapors, with a view to finding a cheap anæsthetic for laboratory work. The results showed that this drug would not be practical, and I have delayed their publication on this account. The renewed interest in the subject, aroused by the employment of petroleum ether in Schleich's inhalation mixture, causes me to submit a brief summary of my work. I employed the commercial gasolene in most of the experiments; in a few I used a purer sample of petroleum ether. The effects were identical. These coal-oil products consist of a mixture of various hydrocarbons of the series CnH_{2n+2} and CnH_2n, the principal ingredient being pentan (C_5H_{12}). The experiments were confined to dogs and frogs.

Effect on Normal Dogs. When the gasolene is poured on cotton, applied to the mouth of a dog, and covered with a towel, the very first effect is a deepening of the respiration. The animal then struggles violently to escape, but the movements soon lose their purposive type, and degenerate (within two to ten minutes) into inco-ordinated convulsions. The animal has apparently lost consciousness, and may be laid on the table. The four legs paw the air as in running. The eyelids, the tail, and the toes twitch. The pupils dilate widely. These rather weak convulsions then assume a stronger and more general type, clonic spasms alternating with tetanus. The neck muscles develop a surprising strength. During this convulsive stage the animal appears quite insensitive to pain, but the corneal reflex is not quite abolished. In the intervals between the general convulsions the animal lies flat, apparently exhausted, with constant twitching of individual muscles.

Death occurs suddenly in two to twenty minutes, heart and respiration stopping at nearly the same time.

The general course of the intoxication was very uniformly, as described, in four normal dogs. In a fifth animal, however, in which death occurred in seven minutes, the convulsions were more of the ordinary asphyxial type.

The autopsy of the animals killed by the inhalation of gasolene gave also very uniform results. The veins and the heart, especially the right side, are considerably distended. The lungs and skeletal muscles are conspicuously pale; the kidneys are injected. The liver, spleen, and intestines appear normal. The blood remains fluid for some time after death. It does not show any striking microscopic or spectroscopic changes.

The previous injection of a heavy dose of morphine does not modify the phenomena if the gasolene is pushed (one experiment); but it makes it possible to graduate the effects and to extend the inhalation over some time.

An experiment made in this manner showed that even a dilution of 1:5 causes some anæsthesia and some convulsions. The anæsthesia was not, however, very deep. Recovery followed promptly on discontinuing the administration. The protocol of this experiment follows:

Experiment. At 10.59 began the administration of 1 volume petroleum ether to 5 volumes of alcohol.

In three minutes there are convulsions, pupils large, some anæsthesia, cornea sensitive.

Discontinued gasolene and started artificial respiration.

In one minute the animal raises its head, and in two minutes it walks around.

At 11.06 administered petroleum ether 1 to alcohol 1.

In twenty-eight minutes twitching of eyelids and lips, tongue blue, general convulsions, pupils rather large, very little anæsthesia.

Artificial respiration begun. The pupils become normal long before the twitchings disappear. In six minutes the animal is still weakly anæsthetic; in eleven minutes it runs about, but is very narcotic.

Effect of the Inhalation of Gasolene on the Circulation and Respiration. For this purpose the animals were first put under a preliminary anæsthesia by a heavy dose of morphine and sufficient A. C. E. mixture. A carotid artery was connected with a kymograph. The trachea was supplied with a cannula, and this was connected with a T-piece, one end of which led to a Woulfe's bottle containing the anæsthetic (or gasolene); the other end leading to a Marey's tambour which registered the respiratory movements. The experiments were made on four dogs.

Mixture of Gasolene 1 *to Alcohol* 8 (*volumes*). The animal remained perfectly anæsthetized for two hours without noticeable

change in the blood pressure. At this time the characteristic convulsions set in. The A. C. E. mixture was substituted, and the convulsions disappeared.

Gasolene 1 *to Alcohol* 5. No effect in fifteen minutes beyond a slight slowing of the heart.

Gasolene 1 *to Alcohol* 3. Immediate weakening of the heart, with fall of the mean blood pressure. Respiration greatly deepened and somewhat slowed.

Undiluted Gasolene. Three experiments showed an immediate weakening and quickening of the heart, with corresponding fall of blood pressure. Section of the vagi in the one experiment in which it was tried did not cause further quickening. The respirations were increased in depth and frequency. One animal died suddenly in ten minutes; the second died in thirty minutes, death being preceded by a sudden fall of blood pressure. The third animal survived over one hour, when it was killed by asphyxia. The last two animals showed a number of the typical convulsions, occurring first respectively three and seven minutes after beginning the administration. During the spasm the heart force increased somewhat, and the blood pressure rose greatly. In the intervals between the convulsions the blood pressure showed a further fall, and muscular twitchings persisted.

It is seen that dilutions of 1:5 are practically devoid of any effect on the circulation. The convulsions occur late. Some degree of anæsthesia can be maintained. With greater concentrations the phenomena consist in an increase of respiration (especially depth) and in a fall of blood pressure. The latter is at least partly attributable to a weakening of the heart. The tonic vagus inhibition is depressed or abolished. The convulsions cause a considerable vasomotor stimulation. Death occurs through vasomotor paralysis (with respiratory failure?), but is very late in some cases.

Effect of the Anæsthetics on the Convulsions. The preceding protocols show that the convulsions can occur after A. C. E. anæsthesia. I have, however, three records in which the convulsions were absent. In one of these asphyxia also did not produce convulsions. It may therefore be assumed that the absence of the convulsions in these cases was due to the persistence of the A. C. E. anæsthesia, which, as we know, lessens the effects of many convulsant poisons.

Effect on Frogs. Three experiments were made. The animals were placed under a bell-jar, the air of which was kept saturated with the vapor by a wad of cotton impregnated with the fluid.

Commercial gasolene was used in the first two experiments. The effects were uniform. The animals at once became excited, tried to escape, wiped the nose with the forepaw, etc. Soon paralytic phenomena were noticed, and in two and one-half to four minutes the animals could not turn when placed on the back, although they made ineffectual attempts. When put in water they could not main-

tain their position, floating with head upward. They would make an occasional fairly powerful stroke, but turn on their side in doing so. Replaced in the jar they would sit flat and execute occasional swallowing movements. In ten to fifteen minutes they would lie flaccid, with legs extended, but react weakly to stimulation. This excitability was also gradually lost, and the animals appeared dead, but on exposing the heart it was still beating strongly. The third frog was treated with petroleum ether, and the same phenomena developed, but more slowly. None of the animals exhibited any convulsions.

Results of Other Investigators. The older literature of gasolene inhalation is summarized by Joseph.[1] The first two cases were of laborers poisoned in cleaning gasolene tanks. The effects were doubtless in large part asphyxial. Some animal experiments of Felix are quoted. Some experiments were also made on criminals, in whom complete anæsthesia was produced.

Elfstrandt[2] investigated pure pentan. The effects on frogs, rabbits, and cats agree with those reported by me. Death occurred by paralysis of respiration, and complete recovery resulted on artificial respiration. The anæsthetic action is comparatively weak. The blood pressure in rabbits is lowered to a greater extent than by ether anæsthetic.

Meltzer[3] notes the convulsions, but saw no anæsthetic effect. With the latter conclusion I must disagree.

Kochmann[4] ascribes to petroleum ether a very weak anæsthetic action.

Conclusions. Gasolene (or petroleum ether) when inhaled has a comparatively slight anæsthetic action. The anæsthesia is, however, very dangerous, since the substance also produces convulsions, weakening of the heart, vasomotor depression, and paralysis of respiration. The kidneys are also irritated. The effects are produced very promptly, and recovery under artificial respiration is also prompt.

The cause of the convulsions is not known. They do not occur in frogs.

[1] C. Joseph. Inaugural Dissertation, Leipzig, 1896.

[2] M. Elfstrandt. Arch. f. exp. Path. and Pharm., 1900, Bd. xliii. p. 435.

[3] S. J. Meltzer, 1898. Cited by W. Meyer, Journal of the American Medical Association, 1903, vol. xl. p. 555.

[4] M. Kochmann. Arch. intern. de pharmacodyn. et therap., 1903, vol. x. p. 347.

A CASE OF SUTURE OF THE HEART, WITH RECOVERY.*

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I am indebted to Professor Keen for the privilege of operating upon and reporting the following case:

T. E., aged twenty years, colored, cook, was admitted to the Jefferson Hospital, February 29, 1904. He had been stabbed in the chest with a long, rusty pen-knife. The stab caused severe pain, but neither felled him to the ground nor caused him to feel faint. He walked without assistance to the hospital, a distance of one and a half squares, then began to feel weak, and was found crawling up the steps leading to the entrance of the hospital. After being disrobed a small wound was found just above the third rib, about one inch to the left of the left margin of the sternum. The wound was surrounded by an emphysematous swelling, and bled continuously, the stream of blood being accelerated by each expiration. The temperature was 97°, and the pulse 80, empty and markedly irregular in volume and rhythm. He lay on the right side, breathing forty times per minute in a short, jerky manner. At times he would complain of a little pain and severe dyspnœa. He was sweating and very pale, and had vomited once. There was neither cough nor blood-spitting. Entire left chest was tympanitic on percussion, except for a small area around the wound. On auscultation the heart beats could be heard indistinctly; there was no bruit nor splashing sound. Under ether anæsthesia operation was begun about forty-five minutes after the infliction of the injury. Time of operation about forty-five minutes. Amount of ether, four ounces. An incision was carried along the second rib for four inches to the sternum, then down the left margin of the sternum to the fourth rib and outward along the fourth rib for four inches. The musculocutaneous flap was dissected back and the opening in the chest found between the third and fourth ribs, the knife having descended after passing through the skin. The exposure was then made more complete by continuing the sternal incision downward for two inches, and the triangular flap thus formed retracted. The third and fourth ribs were severed and forcibly turned toward the right, fracturing the costal cartilages near the sternum. The knife had passed through the pleural cavity and wounded the anterior edge of the left lung. The lung had collapsed into the vertebral gutter, and the pleural cavity contained a large quantity of clotted and

* Read before the College of Physicians of Philadelphia, May 4, 1904.

fluid blood. The opening into the pericardium was easily found by the spurting of blood with each pulsation of the heart; it measured about three-eighths of an inch. The pericardial wound was enlarged in the axis of the heart, and a penetrating wound of the anterior wall of the left ventricle found. This wound was parallel to the axis of the heart, nearer the auricle than the apex, and measured about three-quarters of an inch (larger than either the skin, intercostal, pleural, or pericardial wounds). Bleeding from this wound was free and continuous, whether more marked during diastole I am unable to state, as the heart was now beating very rapidly and resembled a quivering mass of muscle. The wound was closed with a continuous silk suture (six stitches), the sutures being inserted and tied without reference to diastole for the reason already stated. During the suturing the coronary artery was punctured by the needle, causing a profuse hemorrhage which was controlled by an additional suture. The pericardial and pleural cavities were cleared of blood, and the pleural cavity was irrigated with salt solution. The pericardial wound was sutured with a continuous silk suture, a small opening being left at the lower end for the passage of a gauze drain. No attempt was made to suture the lung (which was not bleeding) nor the parietal pleura. A gauze drain was also placed in the pleural cavity, gaining exit at the lower part of the primary incision. The severed ribs were approximated and the soft parts sutured with silkworm-gut. During the operation twenty-four ounces of salt solution containing adrenalin were injected into the circulation and strychnine and atropine were administered subcutaneously. After the operation the foot of the bed was raised, external heat applied, the extremities bandaged, and owing to the violent struggling of the patient morphine was given. Temperature, 100.4°; pulse, 150; respiration, 32.

Second day: Temperature, 103.4°; pulse, 130; respiration, 56. Dressing saturated with blood-stained fluid. Unproductive cough. Strychnine, whiskey, codeine. Delirium, subsultus, carphologia. Great pain in left chest, garrulous wound.

Third day: Temperature, 100°; pulse, 130; respiration, 46. Drains removed and replaced between the edges of the skin wound because of oozing of blood.

Fourth day: Temperature, 102°; pulse, 140; respiration, 52. Passage of air through the external wound has ceased. Ammonium carbonate and digitalis.

Fifth day: Temperature, 102°; pulse, 130; respiration, 60. Examination of the chest reveals dulness, rough breathing, and crepitant rales over the lower part. Blood: erythrocytes, 3,630,000; leukocytes, 38,800; hæmoglobin, 58 per cent. The chest was explored with a needle, with a negative result.

Sixth day: Temperature, 102.8°; pulse, 140; respiration, 48. Pus under skin flap; removal of several stitches.

Seventh day: Temperature, 103.6°; pulse, 140; respiration, 52. Cough continues; little pain.

Eighth day: Temperature, 103°; pulse, 150; respiration, 50. More profuse discharge of pus from the wound.

Ninth day: Temperature, 103°; pulse, 136; respiration, 48. Chest again explored for pus, with negative result.

Tenth day: Temperature, 103°; pulse, 128; respiration, 52. Prolonged paroxysm of coughing.

Eleventh day: Temperature, 103.4°; pulse, 130; respiration, 50. Remaining stitches removed.

Twelfth day: Temperature, 103°; pulse, 128; respiration, 50.

Thirteenth day: Temperature, 100.8°; pulse, 120; respiration, 40. Small slough separating from the skin-flap.

Fourteenth day: Temperature, 100°; pulse, 120; respiration, 40.

Fifteenth day: Temperature, 101°; pulse, 120; respiration, 28. Cough almost gone; never any expectoration. Thereafter the temperature, pulse, and respiration gradually fell until on the twenty-second day the temperature registered 99°, the pulse 98, and the respiration 20. Subsequently the temperature, pulse, and respiration remained below these points. On the thirty-fifth day the patient was allowed out of bed. On the fifty-sixth day the patient was discharged to return to the Out-patient Department for dressing, a small sinus leading down to the point where the ribs were severed, still persisting; this sinus closed a few days later. The ribs have united firmly, with little callous formation. The pulse varies between 80 and 90. Adventitious sounds have never been heard in the heart. The left chest expands very little on inspiration, and slightly roughened breathing, but no rales, can still be heard.

In olden times a wound of the heart was considered synonymous with inevitable and immediate death. Ellsberg[1] tells us that prior to the sixteenth century Hippocrates, Celsus, Paul of Ægina, Roland, and Lanfranc all mention heart wounds, and agree that they are invariably fatal. In the early part of the sixteenth century Fallopius[2] studied the subject, with a view to recognizing the cavity injured, and Jacob Hollerius made the assertion that a wound of the heart was not necessarily fatal. Later in the century bullets, arrowheads, and other foreign bodies were found in the hearts of animals which had continued to run for some time after receiving their death wounds, and tales were told of men who during the intoxication of battle continued to fight after being stabbed through the heart. Toward the end of the century Ambroise Paré[3] related the oft-quoted case of the Turin gentleman who received a rapier thrust below the left nipple during a duel, and who made several passes and pursued his slayer 200 paces before falling to the ground a corpse.

In 1642 J. Wolf[2] gave the first reliable account of the healing of a wound of the heart. Morgagni[2] (1761) stated that the cause of death in many cases was compression of the heart by the effused

blood, a theory which has since been converted into a fact mainly by the observations of Rose and the experiments of Cohnheim. It is interesting in this connection to recall the fact that Morgagni died of rupture of the heart.

Sherman[4] says Desault laid down the rules for pericardotomy for empyema in 1798, and it took surgery ninety-eight years to pass from the pericardium to the epicardium across a space that is such only potentially.

Benjamin Bell[2] (1783) did not believe healing could occur. A. Richter[2] (1786) considered the probe dangerous, and insisted upon absolute rest and free bloodletting. Larrey and Dupuytren laid down many rules for treatment. During the seventeenth and eighteenth centuries papers would appear describing cases in which protracted periods intervened between the injury and dissolution.

In the beginning of the nineteenth century Jamain, Zannetti, and others wrote on the viability of patients after heart wounds; but it was not until 1867, when George Fischer[5] published his classical study of 452 human cardiac wounds, that a firm foundation was laid for the evolution of the surgery of the heart. Fischer clearly established the fact that an individual might exist for hours or even days with a wounded heart; and that, indeed, in from 7 to 10 per cent. of the cases the wound heals and the patient actually recovers. Loison and Ollivier collected additional cases and corroborated the findings of Fischer. Ninni[6] states that according to the statistics of Jamain, Fischer, Lantenelet, and Zannetti, death is instantaneous in 18 per cent. of the cases.

Up until the closing years of the nineteenth century the treatment of wounds of the heart consisted in the application of an occlusive dressing, absolute rest, ice or blisters to the præcordium, sedatives, such as veratrum viride, digitalis, opium, and venesection. Rose[7] advised paracentesis of the pericardium or pericardotomy to relieve compression of the heart the result of a wound. In 1881 John B. Roberts suggested the propriety of attempting to suture a wound of the heart. Later Koenig and Delorme voiced the same opinion. The idea, however, was generally regarded as the wildest fancy of ultra-enthusiasts. Billroth declared that no surgeon who wished to preserve the respect of his colleagues would ever attempt to suture a wound of the heart. Riedinger (1884) considered the proposition below the dignity of mention. Tillmanns was convinced of the hopelessness of surgery when confronted with a bleeding heart. That the heart could be exposed and manipulated has been demonstrated by many experimenters. In 1894 Kronecker and Schmey[1] discovered that this organ might be punctured with but little interference with its action, except when a spot in the interventricular septum was touched, when immediate death ensued (Kronecker's co-ordination centre). In 1895 Rosenthal[1] essayed to treat an experimental wound of the heart by direct means—he used

a tampon of iodoform gauze, and the dog survived. During the same year Del Vecchio[1] was the first to suture the canine heart with success. In 1896 Salomoni[1] and in 1897 Bode[1] successfully closed wounds of animal hearts by suture.

Since then there have been many experimental investigations into this subject. The conclusions of Elsberg,[1] which may be taken as representative of the findings of the experimenters, are as follows: That the heart could be grasped with the hands or forceps and gently compressed, with no appreciable difference in its action, and that it could be penetrated by a needle and knife, producing only a temporary irregularity of its action; that penetrating wounds produced during systole bled more than those produced during diastole, and that wounds of the ventricles produced during systole were larger than those produced during diastole; that oblique wounds bled less than perpendicular wounds; that wounds of the right ventricle were more dangerous than those of the left because the wall of the right ventricle was thinner, and also because the blood in the right side of the heart coagulated more slowly; that wounds of the heart heal kindly and that the cicatrix is usually complete in about fourteen days; that interrupted sutures are better than continuous ones; that the tissue included in the suture always atrophied, and was replaced by scar; a smaller number of muscular fibres was included in the interrupted than in the continuous suture, thus producing less atrophy and less scar tissue; that superficial sutures were less likely to tear out than deep ones, and that the sutures should be inserted and tied during diastole because of the danger of their tearing out if tied during systole.

After the road had been paved by the knowledge that patients would often live long enough for operative interference, and that the heart would tolerate manipulation, two unsuccessful attempts were made in 1896 to close human cardiac wounds by suture, one by Farina and one by Cappelen, and in 1897 Rehn published the first successful cardiorrhaphy in man. Including these cases and the one reported in this paper, I have been able to find 60 cases with the surprisingly high recovery rate of 38⅓ per cent.

Wounds of the heart may be produced by penetration from without, as gunshot or stab wounds, or by fractured ribs, and by foreign bodies from the œsophagus, stomach, or bronchus. The heart may burst as the result of blunt force to the thorax or epigastrium with or without laceration of the pericardium, and it may rupture spontaneously (disease of myocardium or coronary artery, neoplasms, gummata, echinococci, abscess, aneurysm, etc.). That an attempt should be made to save as many of these cases as survive for a sufficiently long period of time after the accident needs no argument. Of the cases thus far recorded, 55 were stab wounds and 5 gunshot wounds. Two of the gunshot wounds recovered (Launay, Noll) and in two of the fatal cases the posterior wound was not

sutured (Bufnoir, Stern). As late as 1903, however, Wolff[8] advises expectant treatment in gunshot wounds of the heart.

The symptoms are those of acute anæmia or of compression of the heart, depending upon the escape of blood into the pleural cavity or externally or upon its retention in the pericardium. In some cases the patient may walk or even run for a considerable distance before falling to the ground. In a recent stab case in Philadelphia the patient was examined by a careful and competent surgeon, who regarded the wound in the chest as trivial because of the absence of symptoms. The patient died within twenty-four hours and an autopsy revealed a punctured heart. On the other hand, a patient may present marked symptoms without a serious injury. During the past year I was called to the Pennsylvania Hospital to see a boy who had been stabbed in the cardiac region. He presented all the classical symptoms of severe shock. Under a local anæsthetic the wound was enlarged and found to be non-penetrating. His symptoms disappeared in a few hours. In any case there may be nervous symptoms, such as vertigo, syncope, convulsions, vomiting, or hemiplegia (Pirogoff). The nervous phenomena are said to be more common in injuries to the left ventricle, and to be due to anæmia of the spinal cord. Respiratory difficulties are more marked in wounds of the right ventricle, but may be due to nervous influences, pneumothorax, or compression of the heart. Hæmoptysis is rare, even if the lung is injured.

When the blood escapes into the pleural cavity (the pleura was injured in 57 of the 60 cases, 95 per cent.) there will be in addition to the symptoms of anæmia the signs of a pneumohæmothorax. Palpation may detect the apex beat. A splashing sound indicates blood and air in the pericardium. A whizzing sound due to the presence of air in the pericardium is also described. In some cases a friction sound may be heard, and in others a bruit not unlike that heard over an aneurysm. The heart is apt to be irregular and in many cases the pulse is below 100°.

When the bleeding is external the stream may be continuous or in jets. Slight increase in cardiac dulness is to be expected. The respiration may be quiet until near the end, and physical examination of the lung may reveal little abnormal.

When the blood is confined to the pericardium the pulse is exceedingly feeble, and the apex beat can neither be felt nor heard. There may be a splashing sound, disappearing with the filling of the pericardium, at which time the area of precordial dulness will be vastly increased. The patient is unconscious, and may regain his senses on providing an exit for the blood. Cohnheim demonstrated by animal experiments that the pressure manifested itself first on the auricles and the origin of the great veins, producing venous stasis; this may increase to complete obstruction to the flow of blood, and is manifested by dyspnœa and cyanosis. The ventricles pump themselves dry, and the heart finally stops.

Death ensues as the result of anæmia, compression of the heart, or later from sepsis or functional incompetence. Izzo[10] reports a case of stab wound of the left ventricle which was discharged cured on the twenty-eighth day. A few hours later the patient died while lifting a heavy body, the scar having ruptured. The possibility of embolism from air or clot should also be thought of.

As may be seen from the foregoing, a diagnosis of injury of the heart may be difficult or impossible without exploration. The location of the external wound is no sure guide. Of the external wounds in the 60 cases, thirty-nine were on the left side, between the second and seventh ribs, sternum and anterior axillary line, two were in the left midaxillary line, two to the right of the sternum, one in the epigastrium, one under the left costal arch, and fifteen not mentioned. It may be stated, however, that any penetrating wound in the præcordium is almost sure to injure the pericardium or the heart. External bleeding may be profuse and spurting from a wounded intercostal or internal mammary, and may be absent in a punctured wound of the heart. Although justified by Rehn, the use of the probe is generally condemned. The statement that the blood coming from the external wound will be bright red when the left heart is injured and dark in color when coming from the right heart is not to be relied upon. Neither can the size of the wound in the heart be predicted with certainty by the size of the external wound nor the cavity injured by its location. In the present case, for instance, the cardiac wound was larger than the external wound, the knife probably entering the heart at the beginning of systole, and as the heart swung forward added an incised wound to the stab, and the location of the external wound suggested a wound of the auricle rather than the ventricle. Of the 60 cases, the left ventricle was wounded thirty times, with fifteen recoveries; the right ventricle twenty-one times, with seven recoveries; the right auricle once, resulting in death; the left auricle once, resulting in death; the apex three times, with one recovery, and in four the chamber wounded is not known. The size of the wound in the heart muscle varied from 0.5 cm. to 7 cm. The only safe procedure in doubtful cases is to enlarge the wound, ascertain if it penetrates the chest wall, and if there be symptoms of hemorrhage or "heart tamponage," operate.

Although the cases operated upon after the lapse of several hours show a larger proportion of recoveries than those operated upon earlier, operation should be undertaken as quickly as possible after the injury. Of the 60 cases, the time elapsing between the injury and the operation is not given in 29, 11 of which recovered. Of the remaining cases 16 were operated upon within one hour, with 4 recoveries, 1 in three and three-quarter hours with recovery, 4 between three and four hours with 1 recovery, 1 in five hours with recovery, 1 in six hours with recovery, 2 in eight hours with 1 recovery, 2 in twelve hours with 1 recovery, and 3 after twenty-

four hours with 2 recoveries. This gives a mortality of over 76 per cent. for those operated upon within four hours, and a mortality of 30 per cent. for those after four hours. In looking over the causes of death in these cases, and leaving out of consideration 2 cases in which the interventricular septum was cut, it may be noted that of the cases operated on under four hours $35\frac{5}{7}$ per cent. died within twenty-four hours, and of those operated upon after four hours $33\frac{1}{3}$ per cent. died within twenty-four hours. An individual who survives a heart wound for a number of hours has a fair chance to recover with operation, and perhaps without operation, but of the cases which would succumb within a few hours many will be saved by prompt intervention.

The advice given by Rydygier[11] to allow a knife which may be found sticking in the chest to remain until ready to suture is questionable. It is easy to understand how the blade might produce further laceration of a beating heart.

An anæsthetic should always be employed unless the patient be unconscious. Ether was employed in the present case, because it was believed to be safer than chloroform. Of 4 cases in which ether was employed, 2 died, 1 on the table; of 11 cases in which chloroform was used, 4 died, 1 on the table; and of 11 cases in which no anæsthetic was given, 6 died, 2 on the table. Of 2 cases in which it is simply stated that an anæsthetic was administered, both died, 1 on the table.

The heart may be exposed by the extrapleural method or by the transpleural method.

Among those who have employed or who advise the extrapleural method are Rydygier, Pagenstecher, Napalkow, Wehr, Giordano, Podrez, and Nietert. Rydygier[11] advises a horizontal incision at the upper border of the third rib, extending from the right of the sternum to the left costochondral joint, then obliquely downward along the outer ends of the costal cartilages as far as the fifth interspace. The third, fourth, and fifth costochondral articulations are divided, the sternum severed subperiosteally and the flap turned to the right. Giordano suggests a vertical incision along the right margin of the sternum, with the division of the second and third cartilages; from each extremity of the vertical incision a transverse cut is made across the sternum, which is then divided and the flap turned to the left by luxating the cartilages. Podrez begins an incision in the second left interspace one and one-half inches from the sternum, carries it as far as the midsternum, then downward to the level of the seventh cartilage and outward along the seventh rib. The sternum is divided at either end of the longitudinal incision and the flap turned to the left. Nietert[12] cuts from the right border of the sternum to one inch to the left of the sternum on a level with the third rib; a similar incision is made on a level with the base of the ensiform, and the left extremities of these incisions are united by a

perpendicular incision. The fourth, fifth, and sixth ribs and the sternum are divided and reflected to the right.

Among the transpleural methods are those of Del Vecchio, Parlavecchio, Farina, Rehn, Cappelen, Parozzani, Giordano, Ramoni, Ninni, and Rotter. Del Vecchio outlines an H-shaped incision: the vertical limbs correspond to the left sternal and mammary lines, and the horizontal portion to the fourth interspace. The fourth, fifth, and sixth ribs are resected, one flap being turned upward and the other downward. Farina, Rehn, Parlavecchio, and Cappelen resect one or more ribs. Parozzani made a triangular flap, one side of which extended along the left margin of the sternum from the fifth interspace to the ninth rib, the second side from the upper end of this incision outward for 3 cm.; the sixth, seventh, and eighth ribs were cut and the flap turned outward. Giordano incised in the third interspace, sectioned the third and fourth ribs, turning the one upward and the other downward. Ninni advocates an incision along the sternum from the third to the sixth rib and the same length in the mammary line, joining these by a horizontal incision in the fifth interspace. The intervening ribs are cut and the flap turned upward. Rotter cuts outward from the left border of the sternum along the third rib for two inches, then downward parallel with the left border of the sternum to the sixth rib, thence along the sixth rib to the sternum. The third, fourth, and fifth ribs are severed and the flap turned toward the right. He also advises the same procedure on the right side in cases in which the wound is on the right. The opening was made in the right chest in 3 cases only (Watten, Ninni, Barth).

The extrapleural method will be indicated in cases in which the wound does not involve the pleura, and in which the patient's condition is such as to sustain an operation protracted by the small opening in the chest wall, and by the careful manipulations necessary to avoid the pleura. This will be rare; in 3 cases only did the pleura escape injury (Pagenstecher, Nietert, Gibbon). Rehn thinks it advisable to incise the pleura to avoid negative pressure from aspirating air into the mediastinum, causing the blood to foam.

An atypical osteoplastic flap with the base toward the sternum either in the right or left chest, according to indications, and including as many ribs as may be necessary for proper exposure, usually from two to four, will probably be used in most of the future cases.

The wound in the lung ceases to bleed as a rule when the lung collapses and needs no treatment; if bleeding, it may be sutured.

The wound in the pericardium is enlarged in the axis of the heart by tearing or cutting, and the sac cleared of blood with the finger. In several of the cases attention is called to the fact that the blood coagulated behind the heart. In experimental work Ricketts found that collapse of the lung would congest the heart, and that exposure

caused it to dilate because of the lack of support of the pericardium and chest wall.

The bleeding from the heart may be controlled by a finger, and the heart may be steadied by the fingers, by forceps, or by sling sutures. In the present case a suture was inserted at the upper end of the wound, tied, and used as a tractor for the insertion of the remaining stitches. In 2 cases the sutures tore out (Walker, Zulehner). Should the heart cease to beat during the manipulation it should be sutured quickly and massage performed. The use of gauze packing will probably never be indicated; to be efficient it must be firm, and to be firm it must exert injurious compression. A round, curved, intestinal needle is generally recommended. Silk was employed in 26 cases with 2 recoveries, catgut in 9 with 5 recoveries, celluloid in 1 with recovery, and in 24 the suture material is not known. The highest number of sutures employed was eleven. Silk has the advantage of being easier to manipulate and more certain to hold. It has been proven that catgut will last long enough for the repair of the wound. Silk was used in the present case because of the fear of untying of the knots by the constant gyrations of the heart. The continuous suture is mentioned in 3 of the cases with 2 recoveries. It may be applied more rapidly than the interrupted, and presents fewer knots on the surface of the heart. The sutures are inserted at intervals of one-eighth of an inch deeply into the muscle, but must not penetrate the endocardium. In dogs Sherman[4] found it a difficult matter to penetrate the endocardium with an ordinary curved needle. After tying, the ends should be cut off one-quarter of an inch from the knot to guard against untwisting. Diastolic suture is difficult and unnecessary. One would have to rehearse with a rapidly ticking metronome for a long time before he would be able to accomplish the feat. In dogs Ricketts[14] and Sherman[4] found it impossible. Although Larrey showed many years ago the possibility of recovery after a severed coronary artery, it has been asserted repeatedly that this accident is always fatal. Ricketts demonstrated on animals that either coronary artery may be ligated at any point without death resulting. Of the 4 cases in which the coronary was injured, only 1, the present case, recovered.

Any blood which may be in the pericardium is now removed by the finger or sponge, and the pleural cavity cleared of fluid and clots. The pleura and pericardium may be sutured or both cavities may be drained. Wolff[8] shows that there is no retention of secretion in the pericardium when it is closed. He explains the presence of fluid behind a tampon in Watten's case by the massage of the heart by the gauze. He says the cardiac wound heals quickly and is not infected, the instrument having been cleaned on its way through the chest wall, and he strongly advises suture of the pericardium without drainage. The dangers of the drain are the same

here as elsewhere—*i. e.*, infection and adhesions. Of the 22 cases in which the pericardium was drained, 2 died within a few hours, and of the remaining 20, 10 (50 per cent.) recovered; of the 15 in which the pericardium was closed without drainage, 1 died in fifteen minutes; and of the remaining 14, 7 (50 per cent.) recovered. The question may still be regarded as an open one. In a future case I think I should close the pericardium and drain the pleura through a stab in the back, as the latter cavity is difficult to clear of blood quickly.

Of the 23 cases that recovered after operation 11 are known to have been complicated with some form of infection; in only 1 case is uncomplicated recovery stated. Of the 37 deaths, 16 occurred within twenty-four hours from shock and hemorrhage, and in 2 of these the interventricular septum had been punctured; 3 died on the second day, 2 from the infection of the pleura and 1 unknown; 4 died on the third day, 2 from infection and 2 unknown; 2 died on the fourth day, both from infection, and in 1 of these the tricuspid valve had been injured; 3 died on the fifth day from infection, and 1 on the sixth, 1 on the fourteenth, 1 on the nineteenth, and 1 on the twenty-second day, all from infection; in 5 cases the time and cause of death are unknown.

I append a table of the reported cases. (See pages 442, 443.)

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Table of Cases of Cardiorrhaphy.

Operator and year.	Location of external wound.	Chamber wounded and size of wound.	Time between injury and operat'n.	Anæsthetic.	Suture.	Drainage	Result and remarks.
1. Farina, 1896	Just above margin of left 6th rib, near sternum.	R. v., ¼ in.	Immediately.	.....	3 silk sutures.	Suture of pericardium.	Death 6th day; bronchopneumonia.
2. Cappelen, 1896	4th left intercostal space in midaxillary line.	L. v., 4/5 in.; left coronary artery sever'd	1 hour.	.....	.....	.....	Death 2½ days; pericarditis.
3. Rehn, 1897	4th left intercostal space near sternum.	R. v., 1½ cm.	24 hours.	Ether.	3 silk stitches	Drain of pleura and pericard'm.	Recovery; empyema.
4. Parozzani 1897	7th left intercostal space in midaxillary line.	L. v., ¾ in.	5 hours.	None.	2 silk sutures.	None.	Recovery.
5. Parozzani 1897	3d left intercostal space.	L. v., 3/5 in.	½ hour.	None.	2 silk sutures.	....	Death 24 hrs.; interventricular septum cut, also pleurisy on l. side.
6. Fummi, 1898	Under left nipple.	Apex, cavity not opened.	Several hours.	.....	1 silk suture.	.....	Recovery; empyema.
7. Ninni, 1898	5th left intercostal space, mammary line.	L. v., 1 in.	Immediately.	None.	2 silk sutures.	No drain pericard'm.	Death on table.
8. Parlavecchio, 1898	5th left intercostal space.	L. v., 1½ in.	8 hours.	Chloroform.	.....	No drain.	Recovery.
9. Giordano, 1898	2d left intercostal space.	L. a., 4/5 in.	½ hour.	None.	4 silk sutures.	Drain of pleura.	Death 19th day; empyema and abscess r. lung.
10. Williams, 1898	.....	L v., not penetrating.	.....	.....	.....	.....	Recovery.
11. Nicolai, 1899	4th left intercostal space, mid. between sternum & nipple.	R. v.	1½ hrs.	Yes.	.....	.....	Death after 12 hours.
12. Tuzzi, 1899	4th left intercostal space.	2 wounds, non-penetrating.	.....	None.	.....	Drain of pleura and pericard'm.	Death 22 days; empyema and pericarditis.
13. Longo, 1899	5th left intercostal space 2/5 in. internal to nipple.	L. v.	Immediately.	None.	3 silk sutures.	No drain of pericard'm.	Death in 15 min.
14. Ramoni, 1899	3d left costal cartilage 4/5 inch from sternum	R. v., 2 w'ds, 1 non-penetrating.	.....	None.	4 silk sutures.	No drain of pericard'm, pleura dr.	Recovery.
15. Marion, 1899	Shot through breast.	R. v.	.....	.....	Catgut sutures.	.....	Death.
16. Rosa, 1899	5th intercostal space.	L. v., 3/5 in. not certain it penetrat'd	.....	None.	1 silk suture.	Drain of pleura and pericard'm.	Recovery.
17. Horodynski, 1899	.....	R. v., 1½ cm.	.....	.....	.....	.....	Death.
18. Maliszewski, 1899	....	.....	.....	.....	.....	Drain of pericard'm.	Death; suppurative pericarditis.
19. Maliszewski, 1899	.....	.....	.....	.....	.....	Drain of pericard'm.	Death; suppurative pericarditis.
20. Bufnoir, 1899	6th left intercostal space.	R. v., gunshot, 22 calibre.	.....	... ..	.....	.....	Death; perfor'n of ventricle, and ant. opening only had been sutured
21. Kosinki, 1899	.....	R. v.	.....	.....	.....	.....	Recovery.
22. Pagenstecher, 1899	4th left intercostal space beneath nipple.	L. v., near apex, 1 2/5 in.	2 days.	None.	4 celluloid sutures.	Drain by threads from myocardium.	Recovery.
23. Nanu, 1900	3d intercostal space 4 cm. from edge of sternum.	R. v., 2 cm	.....	.....	2 interrupted sutures. of silk.	.....	Death 5th day from infection of pericardium and pleura.
24. Masselli, 1900	Below and internal to left nipple, cutting 6th rib.	L. v., near apex.	1½ hrs.	None.	2 sutures	Drain of pleura.	Death in 12 hrs.
25. Fontan, 1900	6 wounds between 3d and 7th ribs in cardiac region.	L. v., 12 mm.	6 hours.	Chloroform.	2 continuous catgut sutures.	No drain, suture of pericard'm.	Recovery.
26. Carnoble, 1900	.....	Apex.	.....	.....	Catgut.	.....	Death in 5 days; empyema.
27. Nietert, 1901	Right of sternum.	R. v.	2 hours.	None, unconscious.	2 silk sutures.	Drain of pericard'm.	Death in 33 hrs.
28. Vaughan, 1901	5th left costal cartilage divided.	L. v., 2½ cm.	¾ hour.	Ether.	7 continuous silk sutures.	.....	Death on table.
29. Ninni, 1901	Left of sternum.	R. a.	.....	.....	.....	.....	Death in 4 days; sepsis.
30. Mignon et Sieur, 1901	.....	R. v.	.....	.....	.....	.....	Death.

Operator and year.	Location of external wound.	Chamber wounded and size of wound.	Time between injury and operat'n	Anæsthetic.	Suture.	Drainage	Result and remarks.
31. Fontan, 1901	.....	L. v.	.....	.....	Catgut sutures.	Suture of pericard'm.	Recovery; empyema.
32. Brenner, 1901	Left of sternum near 6th cartilage.	R. v., 7 cm.	Following day.	Yes.	.....	.....	Death on table.
33. Watten, 1901	4th right intercostal space.	R. v., 3½ to 4 cm.	.....	.....	.....	Drain of pericard'm.	Recovery; right pleura wounded, pneumothorax.
34. Lastaria, 1901	.....	L. v.	.....	.....	.....	.....	Death in 12 hrs.
35. Zulehner, 1901	.....	L. v., ½ cm.	.....	.....	.....	.....	Death on table.
36. Zulehner, 1901	.....	R. v. 1 cm.	.....	.....	Catgut sutures.	.....	Recovery.
37. Stern, 1901	.....	L. v., pistol wound.	.....	.....	Unable to suture posterior wound.	Gauze tampon.	Death in 30 min.
38. Pagenstecher, 1901	In heart region.	L. v., left coronary artery injured.	.....	.....	.....	Drain of pericard'm.	Death in 5 days; pus in pleura and pericard'm.
39. Ninni, 1901	.....	L. v.	.....	.....	.....	.....	Recovery.
40. Walker, 1901	.....	L. v., 8 stab wounds.	.....	.....	11 silk sutures.	Drain of pericard'm.	Death in 24 hrs.; pyothorax and pyopericardium.
41. Walker, 1901	Under left costal margin.	Apex r. v.	.....	.....	Suture tore out repeatedly.	Gauze tampon.	Death in ½ hr.; hemorrhage.
42. Nietert, 1902	Left 6th intercostal space to right of papillary line.	L. v., 2 cm.	14½ hrs	Chloroform.	2 silk sutures.	Drain.	Recovery; empyema.
43. Launay, 1902	Left nipple.	L. v., ant. & post. walls, pistol shot.	3½ hrs.	Chloroform.	Catgut suture in each wound.	Drain of both cavities.	Recovery; uncomplicated.
44. Gibbon, 1902	Left præcordium.	R.v., 1.5 c.m.	½ hour.	Chloroform.	1 catgut suture.	.....	Death on table.
45. Hill, 1902	5th intercostal space a little to right of nipple.	L. v., ⅜ in.	8 hours.	Chloroform.	1 catgut suture.	.....	Recovery.
46. Stewart, 1902	4th intercostal space ½ inch left of sternum.	L. v., ⅝ in.	Immediately.	Ether.	6 catgut sutures.	.....	Death in 3 days.
47. Pomara,[15] 1902	.....	.....	.....	.....	.....	.....	Death in a few days.
48. Milesi,[16] 1903	Upper border 6th rib 1.5 cm. from left border of sternum.	R v., 1.5 c.m.	½ hour.	.....	Silk suture.	Drain of pleura and pericard'm.	Death in 15 hrs.; punct. interventricular septum.
49. Giordano[17] 1903	2 wounds, 1 in 4th and 1 in 6th intercostal space.	L. v., 2 cm. long.	.....	.....	2 silk sutures.	Drain.	Recovery; necrosis of ribs.
50. Giordano[17] 1903	6th intercostal space 1 cm. left of nipple.	L. v., near apex.	.....	.....	2 silk sutures.	Drain.	Death in 1½ hrs.
51. Vince,[18] 1903	5th left intercostal space in parasternal line.	L. v., 6 cm., coronary artery injur'd during suturing.	About 12 hours.	Chloroform.	3 silk sutures.	No drain of pericardium, drain of pleura.	Death 2d day; pneumonia and pleurisy.
52. Janari,[19] 1903	3d left intercostal space bet. ant. axillary & mam. lines.	L. v., 2 cm.	¾ hour.	Chloroform.	3 silk sutures.	Drain of pericard'm.	Death in 74 hrs.; pleurisy.
53. Barth, 1903	Epigastrium and through ensiform.	R v., 2 cm.	Soon.	Chloroform.	4 silk sutures.	Drain of pleura and pericard'm.	Death 4th day; sepsis tricuspid valve injured.
54. Barth, 1903	4th left intercostal space 3 cm. from sternum.	L. v., ½ cm.	Soon.	Chloroform.	3 silk sutures.	Suture of pericard'm.	Recovery, with pleurisy.
55. Barth, 1903	3 cm. above and inside nipple.	R. v., ¾ cm.	.....	Chloroform.	5 silk sutures.	Suture of pericard'm.	Recovery, with pleurisy.
56. Schwerin[20] 1903	4th left intercostal space.	R. v.	¾ hour.	.....	3 silk sutures.	Drain.	Recovery; pyopericardium.
57. Noll,[21] 1903	Revolver wound 5th left intercostal space.	L.v., ant. wall sutur'd, post. not ment'n'd.	1½ hour.	.....	.....	Drain.	Recovery; empyema.
58. Wolf,[22] 1903	.....	R. v., 2 cm.	.....	.....	.....	Drain.	Death in 14 days; empyema.
59. Stude,[23] 1904	Left breast.	L. v., 1 cm.	1¾ hour.	.....	Silk suture.	.....	Death on table.
60. F. T. Stewart, 1904	2d intercostal space 1 inch left of sternum.	L. v., ¾ in., coronary artery injured during suturing.	¾ hour.	Ether.	6 continuous silk sutures.	Drain.	Recovery; pneumonia and infection of wound in chest wall.

Cases 1 to 46 inclusive and Cases 53, 54, and 55 are taken from Hill[10] and Wolff.[6]

THE TREATMENT OF PENETRATING WOUNDS OF THE HEART.[1]

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It is difficult for anyone to speak with authority born of experience on the treatment of penetrating wounds of the heart, since opportunity for repair of such injuries is so rare. Dr. Stewart has presented a table of 60 cases, which are all that have been recorded in surgical literature, and but two surgeons have operated on as many as three cases. My own excuse for attempting to discuss this most important subject is the interest I take in it, due to an unsuccessful effort to suture a stab wound of the right ventricle. I have reported this case in the *Philadelphia Medical Journal*, November 1, 1902. This was the fourth case operated upon in this country.

Dr. John B. Roberts was one of the first to suggest the advisability of suture in cases of penetrating wounds of the heart. This he did in a paper read before the Anatomical and Surgical Society at Brooklyn in 1881. It was, however, not until 1896 that the first case of operation for this condition was reported. Dr. Stewart's table, perhaps, does not present all the operations, since no doubt there are a number of unsuccessful cases which have never been put on record. The results obtained in these cases, twenty-three recoveries, certainly teach us that the former surgical attitude toward penetrating wounds of the heart was altogether wrong, and that we should always attempt their repair whenever the opportunity presents itself. It is evident that certain cases are more hopeful than others. Those patients who are able to survive the injury for some hours or even a day are much more likely to recover after operation than those who immediately pass into unconsciousness and present other symptoms of cardiac compression or those of excessive loss of blood. The repair of gunshot wounds of the heart has not been so successful as that of stab wounds, and probably one reason for this is the fact that in the former there are often two wounds. Peyrot says that 17 per cent. of gunshot wounds are double, while only 1.2 per cent. of stab wounds are. In this connection it is interesting to refer to a case which Trendelenburg reports, in which a bullet was lodged in the right ventricle and the patient recovered without operation. The bullet could be seen with the fluoroscope and its movements observed. Later, it became fixed in the heart wall. Strange as it may seem, there are 19 cases

[1] Read before the College of Physicians of Philadelphia, May 4, 1904.

on record where bullets have lodged either in the heart cavities or wall and the patients lived for varying periods. Rickets, in his most exhaustive study of the surgery of the heart, refers to the frequency with which the heart has been found to be most unexpectedly the seat of injury due to its anomalous situation upon the right side or even within the abdomen.

As one would expect to find, the Italian surgeons are those who have contributed most largely to the literature on this subject. The Germans also have reported a large number of cases. Williams, of Chicago, in 1898, reported the first successful case in America. Nietert, of St. Louis, in 1901, lost a patient thirty-three hours after a successful suturing of the heart from suppression of urine, but was able a year later to report a successful case, the second in this country. Hill, of Birmingham, also has recently reported a recovery after operation. The case reported by Stewart is, therefore, but the fourth successful one operated upon in America.

Regarding the technique of repairing penetrating wounds of the heart, it is impossible to lay down any fixed rule, since it must vary largely with the general condition of the patient and the situation of the wound. In my own unsuccessful case I think I lost valuable time in scrubbing the field of operation after the patient was put upon the table, but I should have felt very remorseful had he recovered from his injury and died from sepsis. From a study of the reported cases, however, I would conclude that in patients who are in a desperate condition the part of wisdom would be to expose and repair the heart with the least possible delay. In patients, on the contrary, who have survived the injury for a number of hours or who are not in an immediately dangerous condition, sufficient time should be taken to thoroughly disinfect the field of operation. The question of an anæsthetic is one about which there has been considerable discussion, and here again it is not possible to form any fixed rule, since in the completely unconscious cases an anæsthetic is unnecessary, and in the conscious cases it is as strongly indicated. That the manipulation and suture of the heart itself is not painful is shown in Nietert's first case, where the patient regained consciousness during the introduction of the sutures and conversed with the surgeon during the closure of the wound. Although an anæsthetic has its disadvantages at such a time, the struggling resulting from the exposure of the heart without an anæsthetic carries with it the danger of loosening a clot which may have temporarily occluded the opening in the cardiac wall. This danger can be illustrated in a case of penetrating wound of the heart which healed without operation, and in which the patient died some time later after violent exertion, producing a dislodgement of the hæmostatic clot. The incision and the nature of the flap must vary with the seat of the injury and also with the promptness with which the heart must be exposed. The tendency of most

operators in their first cases has been to resect the necessary amount of bone and cartilage to thoroughly expose the wound. It is the judgment of the most experienced, however, that a deliberate osteoplastic flap with its base at the sternum or beyond the costo-cartilaginous articulations is to be preferred. Having found the wound in the pericardium and opened it, if bleeding is taking place, a hurried digital examination of the heart should be made, and when the opening is found the tip of the finger should be inserted into it and carefully kept in position in order to prevent the escape of more blood. In some instances it has been possible to introduce the sutures while the finger was still inserted in the opening. If this cannot be done two procedures may be followed: that of introducing traction sutures for the purpose of lifting up the heart, and the other, of placing two fingers behind the heart and so bringing it into the wound. Suture during diastole has been strongly recommended by some. Those, however, who have had experience in closing such wounds seem to agree that it makes little difference when the suture is introduced. It seems equally unnecessary to carefully avoid entering the heart cavity with the suture, since a number of experimenters have shown that it is no easy matter to introduce the suture to that depth. It makes little difference what suture material is used, although personally I should prefer chromicized gut introduced on a small, full-curved intestinal needle. When catgut is used, however, care must be taken to make at least three knots, so as to overcome the danger of loosening. Having closed the anterior heart wound a rapid search should be made for a wound of exit; if none is found the pericardium should then be cleared of clots by damp sponging and the pericardial wound closed with or without drainage. If there has been a wound of the pleura, as in most instances there is, the blood should be removed from this cavity and its wound closed with or without drainage. If the pleura has not been involved in the primary injury it is apt to be opened in the exposure of the heart. The question of drainage is one about which there is also considerable dispute. If the operator has been able to thoroughly cleanse the field of operation, and believes that there has been no contamination during the operation, I can see no more reason to drain either the pericardium or the pleura than there would be after opening the abdomen for an intra-abdominal hemorrhage. If, on the contrary, the operation has been done hurriedly and without thorough preparation, then I think that drainage of both the pericardial and pleural cavities should be established. If it should be desired to drain the pleura and not the pericardium, I believe that this had best be done at a point distant from the field of operation, since in this way drainage at the most dependent point can be obtained, and, in case suppuration takes place, infection of the pericardium possibly avoided.

MEDICAL AND SURGICAL CONSIDERATIONS IN PYO-PERICARDITIS, WITH REPORT OF CASES.[1]

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MEDICAL ASPECTS, BY J. A. SCOTT, M.D.

Pericarditis is usually divided into primary and secondary varieties. Primary pericarditis is so rare that it can be dismissed without further consideration. Secondary pericarditis, or that concurrent with or sequent to other diseases, is that commonly met with in practice. This paper deals only with purulent pericarditis of this type.

Frequency of Pericarditis. This is a difficult matter to decide, for statistics vary considerably. Anders' figures, collected to show the frequency of cardiovascular lesions in croupous pneumonia, show in 275 autopsies the presence of acute pericarditis in 14 cases, or 5 per cent., and chronic pericarditis in 11 cases, or 4 per cent. Riesman, in a study of adhesive pericarditis, analyzed 778 necropsies in the Philadelphia Hospital and found 60 cases of pericarditis, 7.7 per cent.; 20 of these were adhesive; very few were purulent. Breitung, collecting 324 cases of pericarditis at the Berlin Charité, found the following figures: serofibrinous cases, 108; hemorrhagic, 30; purulent, 20 (6.1 per cent.); secondary tuberculous, 24; primary tuberculous, 2; partially adhesive, 111; totally adhesive, 23; ossifying, 2. The proportion of cases of pericarditis occurring in autopsy work is given in von Ziemssen's *Handbook* by various authorities as follows: Duchet, 15.1 per cent.; Chamber, 16.2 per cent.; Willigh, 14.1 per cent.; Taylor, 12.5 per cent. G. E. Still, in an article on "Suppurative Pericarditis in Children," finds in 769 autopsies 28 cases of pericarditis, apparently due to pyogenic infection. Twenty-three of the 28 cases occurred in children under three years of age, and 24 of the 28 showed empyema, thick lymph on the pleura, or acute pleurisy. In 13 cases in which the fluid was examined bacteriologically, 11 were due to pneumococcal infection; of the remaining 15, a large proportion were due to the pneumococcus—empyema, pneumonia, and meningitis being associated.

[1] Read before the College of Physicians of Philadelphia, May 4, 1904.

Analyzing the mortality statistics of the Pennsylvania Hospital since the opening of the Ayer Clinical Laboratory, I have found 40 cases of pericarditis in 552 autopsies. Ten were obliterative in type; in 13 the exudate was serofibrinous; in 16 (40 per cent.), purulent; in 1 hemorrhagic. The great discrepancy will be observed at once between these statistics and those of Breitung, in which were found but 20 cases of purulent pericarditis in a total of 324 cases of all varieties. Clinically these 40 cases were etiologically as follows: tuberculous, secondary, 7; rheumatic, with acute or chronic endocarditis, 5; aneurysm, cardiac and abdominal, 2; nephritis, general streptococcus septicæmia, cirrhosis of liver, and secondary anæmia, 1 each; and lobar pneumonia, 22. In all these 22 cases pleurisy coexisted with the pericarditis; in 6 cases both the pericarditis and pleurisy were fibrinopurulent; in 4 each process was fibrinous; in 3 cases purulent pericarditis was associated with plastic pleurisy, and in 3 cases the pleurisy was fibrinopurulent, while the pericarditis was fibrinous. In 2 cases plastic pleurisy and adhesive pericarditis coexisted, and in 2 others the pericarditis was purulent, while the pleurisy was serofibrinous. In the remaining case the pericarditis was serofibrinous, and the pleural effusion was bloody.

Again, recognizing the great frequency of purulent pericarditis in croupous pneumonia, I have gone over the total number of autopsies upon that disease and find them to total 76 cases of croupous pneumonia and 5 of bronchopneumonia. In 38 cases of croupous pneumonia, or exactly 50 per cent., pericarditis has been found; in 20 cases, or 52.6 per cent., the exudate was serofibrinous; in 17, or 44.7 per cent., the pericardium contained a purulent exudate; in one case the pericardium was obliterated (chronic adhesive pericarditis). In none of the bronchopneumonias (non-tubercular in origin) was pericarditis present.

Etiology. Purulent pericarditis is seen in pyæmic diseases—the streptococcal and staphylococcal infections—as a result of empyema, and in perforation of abscesses in the neighborhood of the pericardium; cancer of the œsophagus, cardiac and aortic aneurysm, etc. It is, I believe, commoner during lobar pneumonia than is recognized, and, as the autopsy records at the Pennsylvania Hospital will show, must be responsible for the death of the patient in not a few cases. The filling of the pericardium with exudate during croupous pneumonia is, I believe, not infrequently overlooked. The diagnosis, however, under such circumstances is a difficult one, as will be detailed later.

Bacteriology. The variety of micro-organisms found in purulent pericarditis depends upon the primary infection producing the disease. The purulent form is most commonly caused by streptococci, staphylococci, bacilli coli communis, pneumococci, and the tubercle bacilli. There is no reason why the gonococcus and the typhoid bacillus should not play a part in purulent pericarditis.

When a connection is established between the pericardium and the œsophagus or the lung numerous saprophytic micro-organisms may be found.

SYMPTOMATOLOGY. Symptoms are often difficult to interpret correctly, mainly because of the fact that pyopericarditis is commonly only one part of the symptomatology of such serious illnesses as a general pyæmic state, abscesses of the mediastinum, or pneumococcal and other infections.

General Appearance. The patient usually presents an anxious expression and dusky pallor of the skin, with dilatation of the alæ of the nose. Dyspnœa is usually present, at times extreme. The pulse in these cases is quick, with a sharp rise under the finger, rapid and of low tension; very unlike the pulse of an acute infection. At times the large veins of the neck are much distended.

Pain. Common usually over the region of the heart, but of moderate severity; again, it may be intense and agonizing, radiating over the left chest and down the left arm. It is commonly increased by pressure in the epigastric region. During the development of a purulent pericarditis, and while friction rub is present, the pain is apt to be more severe and disappears to some extent with the presence of a large effusion. In many cases pain in the epigastric region is an important symptom; this is accompanied with a sense of constant fulness in the same area; nausea and vomiting are apt to be present in this type. The vomiting is bile-tinged in some cases.

Dyspnœa is usually present and is disproportionate to the amount of pulmonary involvement and the rate of pulse.

Cough. Often dry, frequent, and distressing. Often non-productive. If the pericarditis is associated with pneumonia the sputum may, of course, be blood-tinged. Aphonia and dysphagia may be present.

Temperature. Fever is, of course, complained of to some extent. The temperature is at times but slightly elevated, though the pericardium may be filled with pus. The pulse is weak, small, and may present an intermittency known as the pulsus paradoxus, a condition in which the radial is either greatly weakened or altogether obliterated during inspiration. Delirium in pericarditis of all forms is common. At times it is active, at other times it is low. It is especially to be found in the rheumatic cases with hyperpyrexia.

PHYSICAL SIGNS. Purulent pericarditis at times develops without the ordinary physical signs of the disease being present, or at least discoverable; that is, though carefully sought for, the presence of friction rubs over any portion of the precordial area cannot be detected. In many cases pericardial friction rubs antedate the presence of effusion. This is certainly so in the serofibrinous cases. They are heard most commonly in the second, third, and fourth interspaces to the left of the sternum, perhaps more frequently over

the base of the heart than at the apex. They are close to the ear, rough in character; sometimes both coarse and fine sounds can be heard. Heard with the systole and diastole of the heart and not always consistent in length or duration. Pressure increases their intensity. Their inconsistency is their characteristic. Change in position alters the character and time of the sound. At times these rubs can be heard over a large area of the chest; under some circumstances as far as each nipple and down into the epigastric region. Friction sounds, of course, disappear with the presence of effusion into the pericardial sac. Under such circumstances a distinct alteration in physical signs occurs. The apex beat, which heretofore was in its normal position, becomes slightly elevated, perhaps to the fourth space, or may disappear altogether. It may, however, still be palpable in the fourth space. The sounds at the apex are distant and weak. With a normal endocardium no valvular murmurs are heard. Frequently, however, in these cases the causative factor in producing the pericarditis also has caused an endocarditis. Not infrequently the two conditions coexist. Valvular murmurs are therefore to be heard at the areas affected. Coincident with the disappearance of the apex beat occurs an increase in the precordial area of dulness. This is especially noticeable upward to the left of the sternum, perhaps to the second rib and in the fifth and fourth spaces to the right of the sternum. Impaired resonance or dulness discovered in the fifth or fourth interspaces to the right of the sternum, with decided increase of the left border of the cardiac outline and disappearance of the apex beat with weak or feeble heart sounds, is certainly extremely suspicious of fluid in the pericardium. Under such circumstances other physical signs are apt to be present. Owing to the presence of large quantities of fluid in the pericardial sac there is compression of the left lung, especially the lower lobe, in the axillary region. Here at times can be detected a hyperresonant note. The same pressure frequently will produce an impaired or dull note at the extreme base of the left lung. On auscultation at this point the breath sounds may be bronchovesicular or bronchial. This is a pressure consolidation. With physical signs such as these no hesitancy should be felt in inserting a needle into the fourth or fifth space near the left sternum, especially if the absence of the apex beat is demonstrated. In not a few cases fluid will be secured by exploratory puncture in the fourth or fifth right intercostal space. In some cases, however, the physical signs are extremely difficult of interpretation, owing to the presence of complicating conditions. Thus not infrequently in croupous pneumonia there is fluid both in the chest and in the pericardium. Thus in Case II. an empyema of very considerable size dislocated the heart to the left so that the impulse was visible in the fifth interspace one inch outside the mid-clavicular line. With the evacuation of the empyema the pericar-

dial condition was entirely overlooked, and this probably resulted in the man's demise. In two other cases under observation (Case IV. and one not reported in this paper) there was visible pulsation in the second and third interspaces to the right of the sternum, with the development of (in Case IV.) an enormous shield-like area of dulness between the two nipples, with absolutely clear breath sounds at the bases and axillary region on both sides. These physical signs could only therefore be explained by the supposition that the right side of the heart was adherent to the pericardium or that its pericardial effusion had displaced the heart *in toto* to the right. In the unreported case spoken of, adhesions between the lung and the pleura on the left side were so dense that the presumption is that the suspected pericardial effusion was behind both the lung and the heart, which in turn was displaced considerably to the right.

Temperature. The range of fever in purulent pericarditis is less than one would anticipate. As previously stated, the presence of pus in the pericardium will at times distinctly modify an already pre-existing high temperature. In the first case studied, while the pericardium was filled with the purulent exudate, the temperature was subnormal for a week. In Cases II. and III. the temperature range with the pus in the pericardium was between 98° and 100° F., and 100° and 102° F., respectively. In Case IV. the temperature was high. It is difficult to state the exact time of the onset of the pericarditis.

Pulse. The pulse is weak and of low tension from the start, irregular at times; in some cases influenced by respiration, either partially or totally obliterated. The paradoxical pulse was present in Case I.

Blood. A leukocytosis is produced in all cases. If, however, the pus has been present for any length of time in the pericardium, the leukocytes have a tendency to fall again toward, but do not reach, the normal. In cases with pre-existing leukocytosis—and this is found in practically all patients with purulent pericarditis—a hyperleukocytosis is added. In Case I. the leukocytes jumped from 6600 on the tenth day to 21,000 on the sixteenth day, and fell slowly to 17,050 on the twenty-eighth day. Three blood cultures were negative. In Case II. a leukocytosis of 22,700 was present on the fourteenth day. The pericardium at that time was probably full. On the twentieth day with both pericarditis and empyema present the leukocytes were 12,000. The blood was not counted after operation; no blood cultures were taken. In Case III. the leukocytes on the sixth day were 16,400; on the tenth day, 30,800. At this time pericarditis was diagnosed. Blood cultures on the third and fifth day were negative, but a positive culture was found on the tenth day after pericarditis was present. In Case IV. no cultures or counts were made. The urine is much reduced in quantity in all cases; usually contains albumin, no sugar, and on microscopic

examination shows rather numerous casts; in our case granular casts have predominated, though hyaline were also found. The urea output in Case II. (the fatal case) was 30 grm. in the twenty-four hours.

In conclusion, in pneumonia the cardiac outline should be carefully mapped out at the onset. Any changes either in the size or position of the heart should carefully be watched for. With the development of an empyema more rigid scrutiny of the heart should be insisted upon. The presence of dulness in the fifth right interspace or the dislocation of the heart either to the right or to the left side without a coexisting empyema, should lead one to suspect the presence of fluid in the pericardium, and careful selection of the spot for exploratory puncture should be made.

Diagnosis. Pyopericarditis is to be diagnosed by the following signs: The presence of a primary infection capable of producing pus; the development of a rapid, weak, and at times intermittent pulse, cough, and dyspnœa; pain over the heart and epigastric region of severe nature; a temperature of mild degree, and mental symptoms of varying intensity. Associated with these symptoms pericardial friction rubs over the base or the entire cardiac area may be heard. They are at times altogether absent (Cases I. and II.); then follows the rapidly increasing, pear-shaped precordial area of dulness, extending upward to the left second rib, to the right in the fifth, fourth, and third intercostal spaces, at times reaching the right midclavicular line, and to the left to and beyond the left midclavicular line. It is important to note that the apex beat, if present, is within this area of dulness and not at its extreme limits. The shape of this dull area varies with the amount of fluid in the sac. If the quantity is not large the dull area is pear-shaped with its base exaggerated. If the quantity is large the dulness is almost circular or ovoid at its upper border, the centre of the bow being the sternum. The lower dulness merges with that of the liver or even the spleen, but more often with the dulness or flatness of the consolidated lung or that produced by fluid in the pleura. The apex is either lifted to the fourth space or disappears altogether, or the entire heart is bodily displaced to the right or left, according to circumstances.

The sounds at the apex grow distant and faint and at times can be heard with difficulty. The left axilla presents a hyperresonant note with exaggerated breathing; the left base may show a spot of compression dulness with bronchial breathing. To clinch the diagnosis an exploratory puncture should be made in that portion of the dull area farthest away from the ascertained position of the heart, preferably in the fourth or fifth space to the left of the sternum.

Differential Diagnosis. 1. Serofibrinous pericarditis. 2. Acute dilatation of the heart. 3. Acute catarrhal gastritis. 4. Right-sided or left-sided pleural effusion or empyema, either free or loculated. Some unusual conditions have been mistaken for pericar-

ditis, such as mediastinal tumor, acute endocarditis, cases of aortic regurgitation, and we have recently heard that perforation of the bowel was diagnosed by two very competent observers, the man's condition, however, preventing operation, and the autopsy showing the presence of a purulent pericarditis.

Before considering any of these points in diagnosis the following anatomical belief usually stated in text-books is questioned: That the heart usually or always, in the presence of large quantities of fluid in the pericardium, is pushed away from the chest wall, with the consequent disappearance of the apex beat and weakness of sounds. The heart is fixed at its base by the attachment of its vessels, and this leaves the apex and the ventricles as the movable portion to be effected by pressure from all sides or any side; if, however, adhesions already exist between the pericardium and the heart on either the right or left side a lateral dislocation of the heart will occur; or pressure exerted upon the filled pericardium as a whole may cause a lateral dislocation of the heart; perhaps other unknown conditions within the pericardium may produce the same lateral displacement. We hope in the future to be able, with the kind assistance of Dr. Longcope, to experimentally verify some of these views; as yet we have not been able to do so.

1. Serofibrinous pericarditis is usually the result of rheumatic infection or concurrent with tuberculosis or Bright's disease. The history is of decided importance as the causative factor. The symptoms and signs are, of course, much the same as in purulent pericarditis. You have not, however, the usual chest complications seen in the purulent variety. The temperature is apt to be but slight, and the leukocytosis does not reach such a grade as in the purulent form. This fact, however, is not to be relied upon. Cardiac dilatation is common in the rheumatic pericarditis and endocarditis frequent. Dilatation of the heart is not common in purulent pericarditis. The physical signs in both conditions are similar except that we must recall the fact that purulent pericarditis is seldom present without a purulent pleurisy, a pneumonia, or meningitis, or pus or ulceration near the pericardium. Exploratory puncture settles the doubt at once.

2. Acute dilatation of the heart is a common feature of chronic valvular disease and rheumatic pericarditis, but according to Still is uncommon in purulent pericarditis. It is attended with weak, rapid, and irregular pulse. The cardiac impulse, however, is visible, wavy, and occupies several interspaces, although at times it is not palpable; the impulse may be irregular, now weak and now strong, and can be perceived in the epigastric region. The heart sounds are heard, the first short, sharp, but weak, and not either distant or absent. There is a decided increase in the area of cardiac dulness, which, however, does not extend so high as in pyopericarditis. The second sound is sometimes split with so-called "gallop rhythm."

Careful mapping out of the heart dulness shows the mobility of the heart. In dilatation there is a tendency to venous congestion and dropsy; the liver increases in size, the kidneys fail to secrete, and the lungs fill up. The x-ray examination is a decided help, showing in dilatation a fixed quadrangular shadow; in pyopericarditis a movable upper line of dulness. The blood count will show the absence of leukocytosis in dilatation. When dilatation of the heart occurs in rheumatic pericarditis in a case in which friction rubs have been easily demonstrable, the diagnosis becomes extremely difficult. It rests mainly on the points mentioned above, yet we have seen the diagnosis of acute pericardial effusion with request for immediate opening of the pericardium made by a most able diagnostician, and the operation show an acute cardiac dilatation.

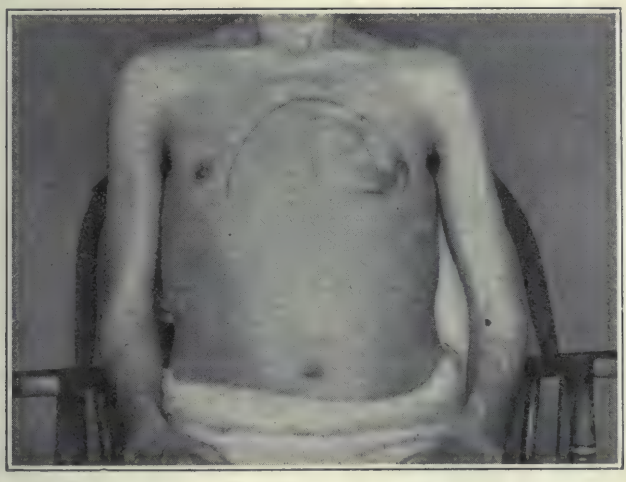
3. Acute catarrhal gastritis presents the history of some causative factor, such as the ingestion of indigestible food, drink, or irritating substance. The vomiting is more or less constant and the pain confined to the gastric area. The temperature is usually high and cough and dyspnœa are not present. The cardiac outline is normal in size and the heart sounds well heard. The blood is of little help, as a leukocytosis may be present in acute gastritis.

4. Pleural effusion, either free or loculated. It is taken for granted that the reader is familiar with the signs of free fluid, be it either serum or pus, in the chest. When this is present in sufficient quantity so that the lower limit of dulness reaches the anterolateral portions of the chest and impinges upon the normal heart dulness, we have a condition which presents many difficulties in diagnosis. If the case has been seen from the start and the size of the heart and the character of its sounds carefully noted, the diagnosis is perhaps not difficult, but when brought face to face for the first time with the presence of large quantities of fluid in the chest with the dislocation of the heart either to the right or to the left and apparent increase in the outlines of the pericardial sac, the diagnosis becomes extremely difficult. Under such circumstances the liberation by either aspiration of the serum or resection of a rib and thorough drainage of the pus is, we think, essential to an opinion. With the relief of the fluid the heart will return toward its normal site. If there remain an unusual area of precordial dulness there is a great probability that the pericardium is also filled. The great frequency of involvement of both the pleura and pericardium in pneumonic cases must be remembered. Of course, change in position of the patient will in large pleural effusion or empyema alter the upper line of dulness. This will, however, give you but little information with regard to the pericardium. Loculated empyema is usually latent and extremely difficult to localize. Unless large it is not apt to dislocate the heart except when present in the anterolateral part of the chest. When so situated the heart is dislocated to the right or left and a visible impulse and apex beat can still be

seen. The symptoms of a loculated empyema, cough, fever, and sweats, with the consequent leukocytosis persist. The pulse remains good, the heart sounds are readily heard and are not weak. There is no evidence of pericardial friction.

CASE I. (Reported in *New York and Philadelphia Medical Journal*, January 30, 1904.)—An Italian laborer admitted to hospital on the sixth day of pneumonia of the right base. Consolidation of left base on ninth day, with an extensive pleurisy. Pericarditis diagnosed on the thirteenth day. Paracentesis performed with immediate relief. Reaccumulation and formal operation on January 31st under local anæsthesia. Slow but complete convalescence at the end of six weeks' time.

M. D., an Italian laborer, aged thirty-six years (Hospital No. 3215), admitted to the Pennsylvania Hospital on January 4, 1903, with history of six days' illness, beginning with a chill, cough, and



CASE I.—The upper line shows the outline of dulness when the pericardium was filled with purulent fluid; the smaller outline of cardiac dulness six weeks after operation.

pain in the right side. On admission physical signs of consolidation of the right base were present. From the start the pulse was weak and heart sounds feeble, though the heart was not displaced and cardiac outline normal. Respirations were rapid (48 to 56), and the leukocytes (ninth day) 8800. On the ninth day the base of the left lung showed signs of consolidation with extensive pleurisy, which was especially marked in the left mammary region. The temperature for the first four days ranged between 103° and 102° F., and gradually fell by the twelfth day to 100° F. in the morning with an evening rise of a degree or more. This low temperature was maintained from this time on. The right base cleared slowly. By the thirteenth day the patient appeared very sick, with grayish

pallor, dyspnœa, and weak, rapid pulse. No pericardial friction was heard, but the pericardium was considered involved by the thirteenth day, empyema of the right base having been excluded by puncture. The apex beat now was neither visible nor palpable and there was impaired resonance in the fifth and fourth interspaces to the right of the sternum. This area of cardiac dulness increased, especially on the right side. The cardiac sounds were very indistinct. The epigastric region was full and very tender. The paradoxical pulse was marked on the eighteenth day of illness, January 16th. The leukocytes, before not increased, had now risen to 18,600. An exploring needle inserted in the fourth right intercostal space showed the presence of light-greenish, turbid fluid, which on culture showed a pure pneumococcic growth. The pericardium was aspirated at the same spot the following day and 420 c.c. of seropurulent fluid were withdrawn, with great relief to the more urgent symptoms. In a week's time rapid reaccumulation occurred, and, as was expected, exploratory puncture now showed thick, yellowish pus in the pericardium. The patient refused operation primarily. Permission to drain the pericardium having finally been secured, Dr. Le Conte operated on January 31st. Chloroform anæsthesia was at first attempted, but resulted in such struggling and cyanosis that local anæsthesia with cocaine was at once substituted and the fifth space incised at the site of the normal apex beat. The pericardium was readily opened and between a pint and a quart of non-odorous pus slowly escaped. The laboratory examination of the fluid showed many leukocytes and pneumococci.

The man was very ill for two weeks after operation, with weak, irregular pulse and but slight fever. From February 22d to 27th there was slight œdema of the face, back, and ankles present, though the urine during this time was free from casts, only leukocytes being present. At no time subsequent to the operation were pericardial friction sounds heard. The drainage tube was removed in twenty-six days and the patient was permitted to leave the hospital on February 23d, fifty-one days after operation.

It is interesting to note in this case the very mild degree of fever present while the pericardium was filled with seropurulent and purulent material.

This patient was seen December 31, 1903, almost a year after operation. He looks well and has gained flesh, and has been doing light work in a store. He states that he is sleepy a good deal of the time and has, on deep inspiration, some pain over the heart and in the back. No dyspnœa or cough is present. Appetite and digestion are good. Pulse is 76, small in volume, and very compressible. There is no œdema of feet. Liver is normal in size.

Inspection of Chest. No venous phenomena of neck; no retraction of interspaces over the cardiac area or behind (Broadbent's sign). The outline of the cardiac dulness is normal. The apex

in the erect position is in the fifth interspace within the midclavicular line. It is definitely movable with change in position. When he lies upon the right side the apex falls at least an inch toward the sternum, and lying on the left side pulsation is visible and palpable one inch outside of the nipple.

Auscultation. First sound is rather short, somewhat liquid, and with weak muscular tone. Second sound is clear; pulmonic sounds are distinct and normal, while the aortic sounds are rather weak and clear.

The features of interest in this case are:

1. The absence of leukocytosis during the pneumonia and its development with the pericarditis.
2. The absence of the pericardial friction sounds, both before and after operation.
3. The absence of fever, subnormal temperature with pus in pericardium.
4. Recovery without the physical signs of an adhesive pericarditis.

Case II.—This case is one of lobar pneumonia complicated with empyema resulting in operation, with death eight days after operation; pyopericarditis overlooked.

The man, S. J. B., aged fifty-two years, was admitted to the Pennsylvania Hospital on December 21, 1903 (No. 2860). His family history is unimportant. Except for a pleurisy four years ago, which lasted three months, has had no serious illness. No venereal history. Formerly drank excessively, but periodically. Smokes freely. Is an attendant for feeble-minded children in Vineland.

Eight days before admission to the hospital he had a severe chill, which was followed by pain in the right side. He had a slight cough with little whitish expectoration. On admission he presented unusually small but equal pupils, urinous breath, with dry, parched tongue. Both the apex and base of the right lung are consolidated; the middle lobe escapes. The liver is increased in size. The abdomen is large; distention marked. The heart is either dislocated or increased in size, the right border being the right edge of the sternum, the left border anterior axillary line, the upper border the second interspace. The sounds are heard distinctly, but are not strong. The apex beat is palpable two inches outside the midclavicular line in the fifth space. No murmurs are present. The temperature on admission and for the first forty-eight hours was about 102° F. On the ninth day there was a fall to 100° F., with subsequent rise (pseudocrisis), and on the eleventh day to 99° F. From this time the temperature is but slightly elevated, about 100° F. The most extreme tympanites developed, which, it is interesting to note, was relieved by eserine. By the twentieth day of the sickness, or twelve days after admission, the signs at the right base indicated fluid. At this time, however, the leukocytes had fallen from 22,700 on the fourteenth day to 12,600. Exploratory puncture on February

5th showed the presence of pus. At this time it was noted that there was impaired resonance in the third and fourth interspaces to the right of the sternum. It was, however, supposed to be due to the line of fluid. The fifth rib in midaxillary line was resected by Dr. Le Conte and showed the presence of a large quantity of thick, yellowish pus in the right pleural sac. He did not do well after the operation, the pulse growing weaker and dyspnœa increasing; the temperature remained low. I regret to say that I did not see him after he was operated upon.

The autopsy showed, in addition to an unresolved pneumonia of the upper and portions of the middle and lower lobe, that the right pleural cavity was well drained, but that a purulent exudate filling the pericardium had been entirely overlooked. The pericardium contained 600 c.c. of thick, yellowish pus.

Case III.—Croupous pneumonia of the left base with the development of pericardial friction on the sixth day of illness; partial disappearance of the friction, with disappearance of the apex beat and great increase in the area of cardiac dulness. No evidence of fluid at the base at this time; incision into the pericardium, evacuation of pus; second operation in eleven days after the first, with drainage of some pus from the left pleura; rapid convalescence and recovery.

D. S. (No. 3141), aged thirty-three years, an Italian laborer, admitted to the Pennsylvania Hospital on January 14, 1904, complaining of pain in the left chest and back, with cough and dyspnœa, and fever of twenty-four hours' duration. On the second day it was evident he had consolidation of the lung involving the left base, faint bronchial breathing being heard at the extreme base and in the anterior axillary line. From the start the pulse was rapid, weak, and compressible. The man was very ill with active delirium. Complained much of pain, especially in the epigastric region and around the left costal margin. On admission the heart dulness was normal in size, no friction sounds were heard, and the heart sounds at the apex were very weak. On January 18th, or the sixth day of the illness, pericardial friction sounds were heard in the left third, fourth, and fifth intercostal spaces. The apex was not visible but palpable in the fourth interspace. By this time bronchial breathing was readily heard all over the left base. On the ninth and tenth days friction sounds were heard at the apex and to the right of the sternum; by the twelfth day there was dulness in the interspaces to the right of the sternum, with very weak pulse, dulness, and absent tactile fremitus in the left axilla. There was no evidence of fluid posteriorly. The leukocytes on the third day of the illness were 17,900; on the seventh day, 16,400; on the tenth day, or the period during which pericardial friction and increase in the area of cardiac dulness occurred, 28,000.

The temperature ran up to 103° F. until the seventh day, when a

pseudocrisis occurred with a fall to 100° F., subsequent rise and fall, and on the ninth day to 99° F. The pericardium was considered filled on the twelfth day. An exploring needle was introduced in the fifth interspace one inch within midclavicular line, and purulent fluid readily secured. Operation was performed within one-half hour under Schleich solution by Dr. Le Conte.

About a quart of pus welled through the incision in the fifth interspace. Upon sudden paroxysmal coughing a large quantity of pus, estimated two quarts, was suddenly expelled from the chest through the incision. It seemed as though an empyema must have ruptured through the incision. It is estimated that three quarts of pus were removed, which showed on culture pure pneumococcus growth. For eleven days the temperature remained between 100° F. in the morning and 102° F. in the evening, with rather rapid pulse (112 to 116); respirations about 32.

Unfortunately, the wound was permitted to close up about six or seven days after this operation. The case about this time was transferred to Dr. Harte's care, and after consultation with him it was considered advisable to reopen the chest to establish drainage, this time into the pleura, with the result that a small quantity of pus was recovered. This was done on February 6th and the twenty-fifth day of the illness. From this time on his convalescence was rapid and complete.

This case has been the subject of considerable discussion among his physicians; it has been questioned if the primary operation opened the pericardial sac, and the opinion expressed by those who did not see the case medically was that we are here dealing with an empyema and not pyopericarditis; that is, a loculated empyema was present with dislocation of the heart to the right side, and that the operation opened up the pleural sac and not the pericardium.

Case IV. (Seen in consultation with Dr. Richard H. Harte in the surgical wards of the Pennsylvania Hospital.)—N. M., an Italian laborer, aged twenty-two years. Both of his feet were frozen and he subsequently developed moist gangrene. Operation (amputation of both feet at lower third leg) after twenty-four days. Profoundly septic at this time. Sloughing of flaps, with granulation. Tardy convalescence. From the middle of February and through March the development of temperature with extensive increase in the precordial area of dulness; lungs clear. Operation, with drainage of the pericardium, on March 14th, with gradual convalescence.

N. M., aged twenty-two years, laborer, admitted to the Pennsylvania Hospital on December 21, 1903. During the cold weather of December this man slept in a barn, in which he was found on the day of admission with both feet frozen. On admission they were perfectly cold and of slate color to about four inches above the ankle. In twenty-four hours blebs formed over both heels, with return of normal color to the skin above the ankles. Moist

gangrene developed in several days' time. By January 10th the lines of demarcation present over both insteps with the development of septic temperature. He refused operation, but finally double amputation was consented to and done on January 14th. The flaps, however, did not do well, sloughed and healed slowly by granulation. By January 29th the temperature reached and remained normal for some time. During February, however, there was a gradual increase in temperature without any unfavorable signs. Pulse and respirations increased in frequency with sweats at intervals. No pain or cough or chill. It is noted, however, that the heart is dislocated to the right and visible pulsation is present in the third, fourth, and fifth interspaces, and the apex of the heart seems to be almost at the right nipple. On March 3d, examination shows that the cardiac dulness extends one inch to the right of sternum. The heart's action is embryonal. There is no cough or expectoration. On March 13th Dr. Harte asked me to see this case with him. There was present a large circular area of dulness over the præcordia, extending one and a half to two inches to the right of the sternum, to the second rib and outside the left midclavicular line. No visible pulsation is present. The heart sounds are loudest to the right of sternum. No friction is present. Paradoxical pulse not present. No venous phenomena in neck. The base and axillary region of left lung are clear. A needle inserted into the fifth interspace within the midclavicular line secures light-yellow, purulent fluid, which on examination shows the presence of streptococci. The following day Dr. Harte resected the fourth and fifth ribs within the nipple and secured a large quantity of pus. The man has slowly convalesced, but the heart has not returned to its normal position. There is still visible pulsation in the third right space, while the apex seems to be in fourth space (adherent pericardium?). No Broadbent sign. The points of interest in this case are:

1. The hæmatogenous or embolic origin of the pericarditis.
2. The unusual delimitation of the pericardial outline.
3. The absence of cough and pain.
4. The differential diagnosis between purulent pericarditis and dislocation of the heart by loculated empyema.

SURGICAL CONSIDERATIONS, BY ROBERT G. LE CONTE, M.D.

In presenting the surgical side of pyothorax the limited time at our disposal will prevent a discussion of the subject in full, and we therefore propose to deal only with three questions of importance to the surgeon: 1st, exploratory puncture for diagnostic purposes; 2d, anæsthesia; 3d, intercostal incision or excision of costal cartilages.

1. *Exploratory Puncture.* Purulent pericarditis cannot be definitely diagnosed unless the fluid is in hand for inspection. For this

reason exploratory puncture is an essential procedure in making the diagnosis. As we cannot tell the presence of pus by the degree of severity of the symptoms, the feeble pulse, and cardiac action, etc., therefore a formal operation for opening the pericardium should not be undertaken until pus has been proved present. One drop is sufficient for a diagnosis, and this can usually be obtained with a slender needle similar to the ordinary hypodermic needle, but somewhat longer.

The three principal dangers in exploratory puncture are wounding the heart, opening a large bloodvessel, and infecting the pleura if septic material be encountered in the pericardium.

A wound of the heart is grave according to its size and depth, but a small wound need not of necessity cause any symptoms. The cavity of the ventricles has been aspirated and life saved in acute dilatation of the heart, and it is a recognized and legitimate surgical procedure. If, therefore, a small needle is used no serious complication need result if the heart is punctured. When the heart is adherent to the anterior surface of the pericardium, or when the diagnosis of pericardial distention is at fault, there is great probability that the heart muscle will be penetrated by the needle. Should the needle puncture the heart it would readily be recognized by the motion imparted to it.

For the same reason the dangers resulting from the wounding of a large bloodvessel are insignificant, and need not be regarded if our needle is small. We can readily avoid the usual position of the internal mammary vessels, and no other vessels need be feared except in the presence of some anomalous distribution.

To appreciate properly the dangers of invading the pleural cavity during paracentesis we must turn for a moment to the anatomy of the part. The anterior mediastinal space, equivalent to that portion of the pericardium which is not covered by the pleuræ, practically commences at the level of the upper border of the fourth costal cartilage and extends downward to the diaphragm. The left pleura recedes much farther from the median line than the right, so that usually the edges of the left pleura do not reach the border of the sternum. For the purpose of obtaining some definite knowledge on the width of the anterior mediastinal space, 11 observations were made on the post-mortem table, and we are indebted to Dr. W. T. Longcope, the pathologist of the Pennsylvania Hospital, for the careful measurements and notes of these cases. From these observations we judge that the average width of the anterior mediastinal space, on a level with the fifth costal cartilage, is from 4 to 5 cm.; but that the space is quite variable is shown by the measurements, in one case being 8 cm. and in another 1 cm. In the latter case, with a width of 1 cm., the edge of the left pleura just reached the border of the sternum. In two other cases, where the widths were 3 and 4 cm., respectively, the left pleura reached nearly to the

edge of the sternum. In the remaining cases the border of the pleura was some distance from the sternum. The right pleura in every instance reached beneath the sternum.

In this region the left pleura is rather firmly attached to the triangularis sterni muscle, but can easily be dissected from it. Its attachment to the pericardium is a little more firm, but in a normal subject it can readily be separated until it dips over the side of the pericardial sac. For some distance, then, dependent upon the position assumed by the pericardium in the left chest, these two layers of parietal pleura are in close apposition. The substance of the membrane is so thin, frail, and translucent that it would be hard to conceive of any inflammation which involved the pericardium that would not also extend to both layers of the overlying pleura and obliterate the pleural space in this region.

The pericardium, although it does not contain elastic fibres, is capable of very great distention, and its cavity will hold quite two litres (Osler). The lungs are displaced and may be thrust far backward and outward in the presence of such distention, but the pleuræ, on account of their attachments, keep their usual relations to the anterior thoracic wall. That pathological lesions change the pleural relations of the pericardium very little is shown by the dissections of Delorme and Mignon (*Revue de chirurg.*, December, 1895, p. 830) in cases of pericarditis and in bodies where fluid was injected into the pericardium. We cannot compare distention of the bladder and its concomitant displacement of the parietal peritoneum with distention of the pericardium, for the peritoneum in the region of the bladder is very loosely attached to the anterior abdominal wall, while the pleural attachment is much more firm to the triangularis sterni muscle and still more firm to the pericardium. We therefore agree with Roberts in believing that Fowler is in error when he states that the boundaries of the pleuræ are greatly displaced in pericardial distention. As the pericardium probably distends equally in all directions the anterior mediastinal space must be broadened to some degree by this portion of the pericardium distending proportionately with the remainder of the walls of the sac. The more the pericardium is distended the greater will be the surface of pleural contact, and when this surface adheres the larger will be the operative field where the pleura can be crossed with safety.

To return to the observations on the cadaver, pins were thrust in the fourth and fifth interspaces to the right and left of the sternum, hugging the border of the sternum as closely as possible. It was found that on the left side the pins traversed the cavity of the pleura in both the fourth and fifth interspaces in one subject, where the breadth of the anterior mediastinal space was 1 cm.; that in two other subjects, in which the anterior mediastinal space was respectively 3 and 4 cm. broad, the pins in the fourth and fifth left interspaces grazed the pleura, but did not penetrate its cavity. In

the other eight cases the pins entered the pericardium some distance from the pleural border. On the right side, in every instance, the pins passed through the pleura before reaching the pericardium.

With such anatomical data we conclude that the point of election for paracentesis, or exploratory puncture, is in the fourth or fifth left interspace, as close to the edge of the sternum as the needle can be made to enter. In this position there is the smallest chance of penetrating the pleura, and the internal mammary vessels should lie well to the outer side of the needle. If exploratory puncture is practised in the fifth right interspace, the point suggested by Rotch, the pleura will almost invariably be traversed. Puncture in the space to the left of the xiphoid cartilage necessitates passing through the diaphragm, and therefore dangerously close to the peritoneum.

The ordinary hypodermic syringe, armed with a needle an inch and a quarter or an inch and a half long, is introduced in the fifth left interspace. If no fluid is withdrawn, and there is no evidence of penetration of the heart by motion imparted to the needle, the fourth interspace should be tried. If this also fails to demonstrate fluid, the same interspace one and one-half or two inches from the left border of the sternum should be tried. If septic material is not found, there can be no danger of infecting the pleura, even though its cavity is invaded. If septic material is present in the pericardium the overlying pleural space is almost certain to be obliterated, and under such circumstances the needle can pass through it without danger of further infection.

2. *Anæsthesia.* In the presence of a large collection of fluid, with feeble heart sounds, the administration of a general anæsthetic becomes very dangerous. In Case I. the patient after four or five inspirations of chloroform became very cyanosed, with feeble, fluttering pulse, and death seemed imminent. Under such circumstances we are forced to use a local anæsthetic, and our experience with infiltrations of Schleich's fluid has proved most satisfactory. In such cases where the heart action has not been seriously interfered with, ether would seem to be the best for general anæsthesia.

3. *Intercostal Incision and Excision of Costal Cartilages.* The choice of operation will be very greatly influenced by the condition of the patient. If a general anæsthetic is contraindicated, excision of a costal cartilage will be dangerous, for under local anæsthesia it cannot be done without causing considerable pain, and severe pain would be very depressing to the heart. Under such circumstances our choice will be limited to an incision through an intercostal space, or aspiration of a large part of the fluid for the purpose of temporarily relieving the embarrassed heart and permitting later the giving of a general anæsthetic.

Incision is certainly as safe as aspiration with a large needle or trocar, and it frequently permits of a recovery without further operative procedure, while aspiration necessitates a later operation.

If the pericardium is much distended with pus the overlying pleural cavity is almost certain to be obliterated, and incision through it can be made without risk.

The point of election for incision is the fourth left interspace, beginning one inch from the sternal border and extending to the normal position of the apex beat of the heart, about one inch internal to the anterior mammary line. The tissues are infiltrated with Schleich's fluid and the incision gradually deepened. When the pleura is adherent it cannot be recognized; but if its cavity is free, and the incision has been carefully deepened, air will rush in as soon as it is penetrated, and before the pericardium has been opened. When pus is reached it is allowed to flow out slowly for fear of embarrassing the heart by the sudden relief of pressure. A rubber drainage tube is inserted and an ample dressing of gauze applied. This is sufficient for the time being, and the question of flushing the pericardium or resecting the costal cartilages may be put off until the physical signs show that the drainage is not good or that the tube is plugged with membranous lymph.

Intercostal incision produces no shock; it is the simplest procedure in grave cases; it permits of a more extensive operation at a later period if found inefficient; it permits the recognition of non-adherent pleural surfaces before the pericardium is opened, and in the majority of cases it will lead to a cure where a recovery is possible from an operative procedure. The question of the recovery of the patient is more dependent upon the cause of the pyothorax and the pathological lesions present in other portions of the body than upon the choice of an operative procedure.

The deductions drawn by Reichard ("Zur Kasuistik der Operationen bei Pericarditis," *Mitteilungen aus den Grenzgebeiten der Medizin und Chirurgie*, No. 7, p. 356), in advocating resection of a rib instead of incision in the intercostal space, do not seem to us to be justified. He collected 33 cases, in 19 of which incision was practised and in 14 resection of a costal cartilage. Of the 19 cases 6 recovered and 13 died, and of the 14 resections 8 recovered and 6 died. From this statement of figures he concludes that the safest procedure is resection. If, however, we examine these cases more carefully we will see that of the 13 cases dying after incision 1 died on the table, 2 others within twenty-four hours, a fourth while the pericardial cavity was being flushed after operation, a fifth some weeks later, following a double empyema operation, and a sixth from joint empyema. These 6 cases would probably just as surely have died after resection, and one is led to believe that perhaps their condition was so desperate that so formal an operation as resection was not used because too prolonged and dangerous. If, then, these 6 failures are subtracted from the 13 deaths, we would have 6 recoveries and 7 deaths following incision. Also, when we examine the cases that recovered under excision, we find

that in 1 the disease was primary in the pericardium, and that 2 others were the result of stab wounds—in a sense, therefore, primary also. Such favorable cases would probably have recovered as rapidly with simple incision, and, if so, by removing them from the tables of the recoveries we would have 5 recoveries with 6 deaths. In other words, the statistics of the two procedures may be regarded as very nearly equal in the same class of cases.

If excision becomes necessary we are inclined to think that the chondroplastic flap suggested by Roberts is better than the removal of one or two costal cartilages. Roberts cuts his flap through the fourth and fifth costal cartilages and turns it upward, using the soft tissues of the third interspace as a hinge. On the normal cadaver it gives a good exposure of the internal mammary vessels and readily permits of their ligation if they cross the field of operation, and the border of the left pleura is easily recognized and can readily be dissected free and pushed aside if its surfaces are not adherent.

CONCLUSIONS. 1. Purulent pericarditis is quite frequently overlooked in lobar pneumonia and in other pyæmic states.

2. Its presence modifies the pre-existing disease to a considerable extent.

3. In diseases with high temperature the presence of purulent pericarditis depresses the fever range and increases the respiratory and pulse rate without sufficient clinical evidence of trouble elsewhere than in the pericardium.

4. It is yet to be proved that the heart, in case effusion is present in the pericardium, is always dislocated backward and upward. It is probable that in some cases the presence of fluid in the pericardium dislocates the heart either to the right or to the left. (This, of course, will occur if previous adhesion between the heart and the pericardium has occurred on either the right or the left side.)

5. The diagnosis once made, the only treatment should be incision and thorough drainage. (Paracentesis will at times relieve temporary urgent symptoms and should be performed without the slightest fear.)

6. That exploratory puncture can be made with safety, and is essential for diagnostic purpose before operation is undertaken.

7. That such puncture should be made in the fourth or fifth left intercostal space, as close to the sternum as possible, with a fine needle.

8. That pericardial dilatation does not alter the relations of the pleuræ to the anterior thoracic wall.

9. In the presence of pyopericarditis the overlying pleural space is usually obliterated by extension of the inflammation.

10. That incision under local anæsthesia is the preferable operation in the majority of cases.

11. That Roberts' chondroplastic flap is preferable to an ordinary excision of costal cartilages when incision fails to give adequate drainage.

PERICARDITIS: ITS SYMPTOMS AND DIAGNOSIS.[1]

By David Riesman, M.D.,
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Pericarditis is, as a rule, more damaging to the heart than endocarditis. It is almost certain to shorten the life of the person afflicted unless an intercurrent disease should anticipate its effects.

Its causes, to which, merely for the sake of completeness, I would briefly refer, are in the main twofold: direct extension and hæmatogenous infection. Traumatic pericarditis is so rare that it may be disregarded.

The pericardium may be involved by direct extension from neighboring structures in the thorax, such as the lung, the pleura, the mediastinal and bronchial lymph glands, and the œsophagus; also from the endocardium or the myocardium, from the great vessels near their origin, and from aneurysms. Inflammatory processes below the diaphragm may likewise cause pericarditis by extension.

Hæmatogenous infection is the most frequent, and gives rise to the type of pericarditis accompanying acute articular rheumatism and other infectious diseases. A form of particular interest is that associated with Bright's disease and uræmia, the true nature of which is still in doubt. Unquestionably, however, its cause is hæmatogenous, and is either a toxin or a bacterium. It may develop in any of the forms of nephritis, but is most frequently encountered in acute Bright's disease, in the early stages of the large white kidney, and in chronic interstitial nephritis. Frederick T. Roberts says that it is almost never found in cases of typical large white kidney. In one of my cases, however, the kidneys were in an advanced stage of chronic parenchymatous nephritis (the so-called large white kidney); but, as the patient had pneumonia also, the share of the kidneys in producing the pericarditic process is not readily fixed.

Nephritic, or uræmic, pericarditis is nearly always of the fibrinous variety, with little fluid; but it may be serous or hemorrhagic. I am not forgetting simple hydropericardium, which is sometimes present in cases of chronic nephritis complicated with general dropsy and effusions into the serous cavities. I have, however, been surprised at the rarity with which hydropericardium occurs when the conditions supposed to favor it, renal and cardiac dropsy, are present.

[1] Read before the College of Physicians of Philadelphia, May 4, 1904.

Pericarditis is quite common in cases of pneumonia, especially when this disease is on the left side. It is frequently overlooked, but should always be thought of as one of the possible causes of so-called delayed resolution, or, rather, delayed crisis. In my experience it has usually been purulent; but it may be serofibrinous. It is generally accompanied with a mediastinopericarditis or a pleuropericarditis of the same nature.

I must say a few words in regard to pericarditis of tuberculous origin. This is usually of the plastic, obliterating variety, but sometimes it is purulent. It is rare, and is commonly overlooked during life; and even after death its true nature may not be recognizable without a microscopic examination.

In taking up now the symptoms and diagnosis I shall not discuss these two aspects of the subject separately, but shall consider the principal features as they present themselves to the examiner.

1. The Friction Sound. This is most marked in acute fibrinous pericarditis, the commonest form. Its site of maximum intensity is to the left of the sternum in the third and fourth interspaces, and sometimes in the second. In rare instances, as in two under my observation at the present time, it is heard first or solely at the apex. It is usually of a churning character, superficial, and markedly intensified by pressure with the stethoscope. It may have a gallop-rhythm, and in pronounced cases it has a peculiar chugging quality, like the noise made by a locomotive just starting to move. If confined to the apex, it may closely resemble a presystolic murmur; while when loudest at the base it may simulate double aortic disease. The character of the pulse, the size of the heart, and the history, together with careful examination so as to discover the second aortic sound, will aid in the diagnosis from aortic-valve disease.

When the friction sound is loud it is often difficult to distinguish existing endocardial murmurs. These may be heard if a double stethoscope is used and no pressure is applied. Pressure brings out the friction sound and thereby renders the murmurs faint or inaudible. I have recently been able to study the heart before the development of pericarditis in two cases. One was that of a young Italian with aortic regurgitation. In the other case, also that of an Italian, there was mitral insufficiency. As the friction sound increased in loudness, the murmurs in both grew fainter and fainter, and at present the aortic murmur is inaudible; while the mitral systolic can be heard when the stethoscope is placed lightly upon the chest. In some cases a mitral murmur, obscured in the precordial area by the confused noise of the friction sound, may be heard in the axilla.

Pleural and pleuropericardial friction must also be differentiated from the ordinary pericardial friction. Both are modified by respiration.

The existence of a friction sound does not exclude the presence of fluid. In one of the cases in which Dr. Roberts tapped and obtained considerable fluid, the friction sound had not disappeared. The fluid is often held in compartments separated from one another by bands or areas of adhesion, which preserve the friction sound. In some cases the friction sound persists at the apex after it has disappeared elsewhere, probably because the greater movability of the apex retards the formation of adhesions.

Friction may cause a palpable thrill. Of my recently observed cases this thrill was present in two out of nine. The loudest friction may, however, be entirely unaccompanied with thrill.

2. Pain and Tenderness. These were present in four of the nine cases. In these four the pain was intense. In three the tenderness was an exquisite hyperæsthesia, so that percussion became torture. In one of the cases the pain was paroxysmal, and was apparently as severe as in angina pectoris, although its direction of radiation was different. It started at the wrists and ran with great violence up the arm and across the shoulders into the chest. In another case there was moderate pain and tenderness in the epigastrium, and in one severe subjective pain in the præcordia and the epigastrium, without any tenderness.

It is not easy to explain why, with no difference in the physical signs, the pain and tenderness should be extreme in some cases and entirely absent in others. It may be that in those with pain there is involvement of the superficial structures, especially the muscles, analogous to that described by Coplin as accompanying pleurisy and pneumonia.

3. The Apex Beat. In the fibrinous form the apex impulse is diffuse, indistinct, and sometimes undulatory, and can usually be appreciated better by touch than by sight. In effusions of any size, it is commonly absent; but a more or less vigorous apex beat is entirely compatible with the presence of a large effusion, as was strikingly shown in a patient that came under my observation at the Polyclinic Hospital. Even when the apex beat cannot be seen, it may often be felt as a distinct shock—a point of importance in differentiating between dilatation and effusion. When the apex beat can be located it is found above the lower level of dulness.

4. Pericardial Effusion. Few conditions are more frequently overlooked than effusion into the pericardial sac. At times the signs are unmistakable, even upon very superficial examination; at other times strong doubt encompasses the diagnosis. The signs to which value should be attached are:

1. The character of the right border of the heart, which becomes convex.

2. A change in the cardiohepatic angle, which, from having been a right angle, becomes an obtuse one.

3. As a corollary, the presence of Rotch's sign, dulness in the right fifth interspace, close to the sternum.

4. An increase in dulness upward as far as the second interspace.

5. Flatness with intense resistance on percussion.

6. The position of the apex beat with relation to the lower boundary of the precordial dulness.

7. The shape of the precordial dulness, which is triangular, or, rather, shaped like a trapezium, with the base downward.

8. Bamberger's sign, a patch of dulness with bronchial breathing near the angle of the left scapula.

9. Ewart's sign, a separation of the first rib from the clavicle, making it possible to feel the former throughout its length.

10. The presence of fluid on exploratory puncture.

The best place for *exploratory puncture* and also for aspiration is still unsettled. There is certainly no one point of election suitable for all cases. When the presence of fluid is suspected and the friction sound is still present over limited areas, it is a good and self-evident rule not to make the puncture where friction is heard; nor should it be made at a point where the heart sounds are very distinct. Another wise maxim is to go in slowly and to arrest the needle as soon as the heart is felt to rub against its point. If the apex can be shown by auscultation—or perhaps by palpation—to be above the level of the fluid it will naturally be perfectly safe to tap below it. This will usually bring the point of puncture in the sixth interspace, about the nipple line. At other times the fourth or fifth interspace on the right may with advantage be selected.

The presence of fluid may be simulated by dilatation, and differentiation of the two conditions is far more difficult than the parallel-column method of text-books indicates. I have mistakenly tapped in a case of this kind, and others have had a similar experience. The position of the apex beat with relation to the lower boundary of the heart is of value in the diagnosis; also the presence of a decided cardiac impulse, especially a pronounced diastolic shock. Search should also be made for Bamberger's sign, referred to above.

Great diagnostic difficulties must arise when the fluid occupies an abnormal position; when, for instance, it is collected on the left side of the heart, in which case the precordial dulness extends into the left axilla and simulates pleural effusion. If the fluid is in the pericardial sac, the dulness rarely extends below the eighth rib in the axillary line. Sometimes only tapping can decide the question. When a pleural effusion is co-existent—and this is not at all uncommon—the discovery of the pericardial effusion is rendered far more difficult. When there is double pleural effusion, the pericardial effusion is usually overlooked.[1]

[1] In one of Thayer's cases, just published (Johns Hopkins Hospital Bulletin, May, 1904), the fluid (over 1200 c.c.) was lying posteriorly to the heart and at the lateral angles of the pericardial sac.

Sometimes pericardial effusions shift with change of posture, especially when the patient is turned to the right. Fluctuation is said to occur at times, but in the cases that I have seen it was not noticed.[1]

Pericardial effusion sometimes simulates *mediastinal tumor.* This is especially the case when the effusion is of long standing. In both conditions there may be dyspnœa, orthopnœa, engorgement of the jugular veins, intense cyanosis, dysphagia, enlargement of the veins of the chest, and extreme flatness on percussion. As at times there is no history suggesting an antecedent pericarditis, suspicion of a mediastinal tumor in these circumstances becomes not unreasonable. A year or two ago I reported a case of this character to the Section in Medicine of the College of Physicians. The patient had the signs that I have mentioned. The cyanosis and dyspnœa were very marked, and the flatness on percussion was most striking. The onset had been insidious, and there was no history of any previous illness. The man was not bedfast, but was able to walk to the Polyclinic Hospital on the clinic days. I took the view that the case was one of either pericardial effusion or mediastinal tumor, although the latter seemed the more likely; but the man died a few weeks later of exhaustion, and the autopsy showed hæmopericardium, the origin of which was not revealed. It is a curious fact that in another case in which the diagnosis of mediastinal growth was for a time entertained, hæmopericardium was also found.

Pericarditis with effusion sometimes simulates *pneumonia.* The distended sac compresses the left lung, and examination of the latter may show impaired resonance and a patch of bronchial breathing in the back. The existence of fever, cough, leukocytosis, dyspnœa, and cyanosis strengthens the suspicion of pneumonia. In a case of this kind that came under my observation at the Philadelphia Hospital, the cyanosis and general prostration were out of proportion to the extent of lung apparently involved. Such disproportion may constitute a point of diagnostic significance.

It is well known that morbid conditions in the chest may cause *pain to be referred to the abdomen,* and give rise to the belief that the disease is located below the diaphragm. I need mention only the so-called "abdominal" pneumonia, which is not rare in children and is also seen in adults. This may resemble appendicitis or perforation of the intestine. Less well known is the fact that pericarditis may cause pain of such severity in the abdomen as to simulate peritonitis.

On the other hand, the interesting observations of Ortner (*Wien. klin. Woch.*, June 29, 1899) teach us that in some cases of peritonitis, chiefly of the hepatic and epigastric regions, a friction sound

[1] In pericardial effusion, just as in hypertrophy of the heart, skodaic tympany may sometimes be detected over the upper part of the left lung.

may be heard over the præcordia, in the total absence of inflammation of the pericardial sac.

A peculiar case, probably belonging to the class described by Ortner, came under my observation at the Polyclinic Hospital in February. A woman, fifty-two years of age, was admitted with severe epigastric pain, tenderness, vomiting, slight jaundice, fever, and leukocytosis. There were no cardiac symptoms, but examination showed the presence of a pronounced friction sound, which was audible from February 3d to February 6th. A few days later a friction sound was discovered in the region of the gall-bladder, extending thence for a short distance upward over the liver. Within a few days this also had disappeared, and the patient left the hospital apparently well.

The only way in which one can escape the error of diagnosing abdominal disease when the trouble is in the chest, and *vice versa*, is by making a careful examination of the thoracic and abdominal organs in all cases.

Even in the early stages of pericarditis signs of *pulmonary congestion* are common, especially on the left side, in the lower axillary region. In three of my cases a distinct generalized *bronchitis* was found.

Fever is, as a rule, present in acute pericarditis, but it has nothing distinctive. When the effusion is purulent the fever may be intermittent, even when the quantity of pus is small. The fever in pericarditis may be present for several days before the friction sound is discovered. Until then the case is usually considered to be one of tuberculosis, sepsis, or typhoid fever. I have thought that in such circumstances the pericarditis probably begins posteriorly, and that the sudden appearance of the friction sound, several days after the onset of fever, is due merely to the fact that the inflammation has extended sufficiently far forward for the friction to become audible.

A curious phenomenon not rarely observed in pericarditis is pronounced *delirium* or other mental disturbance. Da Costa, Balfour, and Musser have made reference to this feature. In one case studied by me with the late Dr. Packard at the Philadelphia Hospital, there was maniacal delirium, which might readily have led an observer less thorough than Dr. Packard astray. Da Costa, in one of his last papers, advised that in every case of acute mania the heart should be examined for pericarditis. The duration of the delirium is variable. In a case of mine, one of tuberculous pericarditis, it extended over a number of weeks and was of a mild character. In his lucid intervals the patient was extremely irritable.

It is difficult to explain the variability in the general reaction of the system to inflammation of the serous membranes. We are accustomed to consider the three serous sacs identical; but pathology proves them to be different, even if histology does not.

The pleural cavity may contain pus for days, weeks, or months without the production of a serious general infection. The peritoneum is a much less efficient guardian of the organism, and suppurative inflammations, as a rule, very speedily influence the condition of the system at large. Acute inflammations of the pericardial sac, whether purulent or serofibrinous, seem to be rapidly productive of constitutional symptoms.

In order to solve these enigmas, we must know:

1. The conditions of lymphatic absorption, both as to direction and as to rapidity.

2. The efficiency of the lymph-gland outposts.

3. The richness in nerve supply, upon which the degree of functional disturbance will depend.

Adherent pericardium more often, probably, than any other important condition comes to the autopsy table undiagnosed. One reason for this is that at times the characteristic signs are altogether wanting. At others, some or all of them are present but are overlooked. Briefly stated these signs are as follows:

1. Systolic retraction of the intercostal spaces.

2. Retraction of the lower portions of the chest in the lateral and posterior aspects—the so-called Broadbent's sign.

3. Diastolic shock or rebound.

4. Absent respiratory movement in the epigastric triangle. The last three are found especially in cases of mediastinopericarditis.

5. Pulsus paradoxus—the so-called Kussmaul's sign—the pulse becoming weaker during inspiration. This is not of much diagnostic value, except when accompanied by inspiratory swelling of the veins of the neck.

6. Diastolic collapse of the veins of the neck—Friedreich's sign.

7. Marked undulation of the heart beat.

8. Early ascites, preceding œdema of the legs.

9. Marked irritability of temper. I have been struck with this, but cannot say that it is either a constant or an important symptom.

10. In rare cases, mild delirium.

For practical purposes the following statements may be made with regard to adherent pericardium. It may be suspected:

1. In cases in which a friction sound has been heard over a great extent of the præcordia and has disappeared.

2. As a probability, in children having a chronic valvular lesion and marked hypertrophy of the heart. In such cases adherent pericardium is commonly found at autopsy. The extreme stretching of the sac and the consequent pressure of the two layers against each other cause alterations of the endothelium favoring a low-grade infection.

3. In adults and children with chronic valvular disease, in whom, with heart sounds of good volume and an impulse of great force, there develop ascites and dropsy of the limbs. In such cases we

may infer that there is something more than the mere valvular lesion. The ancillary factor may not always be adherent pericardium; it may be a fibroid myocarditis, but it is often the former.

4. In the cases of so-called quiet ascites, chiefly occurring in young subjects, in which cirrhosis of the liver and tuberculous peritonitis can be excluded. I have reference to the so-called pericarditic pseudocirrhosis, a subject ably discussed before this society by Dr. Kelly.

Since the beginning of the year to the present time, 9 cases of acute pericarditis have come under my observation: 2 I saw through the courtesy of my colleague, Dr. Thomas G. Ashton, at the Philadelphia Hospital; 2 occurred in my own wards in that institution; 3 were observed during my term of service at the Polyclinic Hospital; 1 was in a patient of Dr. Francis T. Stewart, and 1 I saw in consultation with Dr. L. Podolski. Of these 9 cases 3 were in the female and 6 in the male sex; 4 of the patients were colored persons; 3 were tapped—1 with a negative result.

Etiologically the cases may be classified as follows: Probably of rheumatic origin, 4; associated with pneumonia and nephritis, 1; secondary to operation for the radical cure of hernia, 1; secondary to gallstone colic, 1; of unknown origin, 2. Of the 9 cases, 7 were associated with endocarditis and 2 were unaccompanied with any evidence of endocardial lesion; 2 ended fatally, the autopsy showing fibrinous pericarditis with adhesions.

I have confined myself to a mention of these few details in regard to the cases so as not to lengthen the paper unduly. Those interested in the subject will find these cases more fully discussed in the forthcoming volume of the *Transactions of the College of Physicians of Philadelphia*, 1904, vol. xxvi.

TWO CASES OF PARACENTESIS OF THE PERICARDIUM.[1]

By John B. Roberts, M.D.,
PROFESSOR OF SURGERY IN THE PHILADELPHIA POLYCLINIC.

The glory of modern surgery can be appreciated only by practitioners who, in their youth, were familiar with the almost universal occurrence of operative sepsis. Surgical timidity, due to "inflammatory fever" and its results, made the experienced surgeons of our youthful days skeptical of the opinions of those of us who saw the coming of the new era.

The contention that trephining was not a serious procedure and ought to be adopted in nearly all fractures of the cranial vault[2]

[1] Read before the College of Physicians of Philadelphia, May 4, 1904.

[2] Roberts, Operative Surgery of Human Brain, Transactions of the American Surgical Association, 1885.

aroused opposition, and the advocacy of suprapubic cystotomy in preference to perineal incision was regarded as foolishness.[1]

So it was with my proposition that the diseased pericardium should be treated as the pleura in similar pathological conditions. That the pericardium should be promptly aspirated (1876), if it contained a serous or hemorrhagic effusion unaffected by the administration of drugs, and that it be kept empty by incision and drainage (1876), if the fluid contents were purulent,[2] was doubted. These procedures are now routine operations. It then seemed hazardous to incise the chest wall and pericardium to clear up a doubtful diagnosis of dilated heart or pericardial effusion (1881).[3] The advocacy of heart suture as a therapeutic procedure for wounds of the cardiac wall (1881 and 1883) seemed in 1882 to be a youthful indiscretion, if one could judge from the tone of the Fellows of this College.[4] A formal method of attacking the pericardium and heart by a trap-door resection of the costal cartilages, devised in 1897,[5] was, however, the outcome of these studies.

This obstructive conservatism is, however, the usual attitude of mind of the middle-aged, and surgeons of that period of life need to bear in mind that most of what the profession learns is taught by young men.

To-night several cases of pericardicentesis and of pericardial drainage have been reported, and two Fellows, Dr. John H. Gibbon and Dr. Francis T. Stewart, have each added to surgical literature an instance of heart suture for penetrating wound. In Dr. Stewart's case the patient recovered. I feel honored that both are ex-resident physicians of the Polyclinic Hospital.

Through the courtesy of Dr. David Riesman I recently had the opportunity of aspirating the pericardium in two patients with pericarditis, and desire to join him in the record of the cases. Both were tapped with the pericardial aspirating trocar devised and described in 1877 and 1881.

Roberts' pericardial aspirating trocar, consisting of a hollow needle and an internal cannula with flexible end.

Case I.—The patient, a colored woman, had been admitted to the Polyclinic Hospital the day before with pericarditis and bronchopneumonia.

Tapping was done March 9, 1904, at 6 P.M., in the fourth left

[1] Roberts, Transactions of the American Surgical Association, 1884, p. 169.
[2] New York Medical Journal, December, 1876.
[3] Annals of Anatomy and Surgery, December, 1881, p. 250; Medical News, January 13, 1883.
[4] Transactions of the College of Physicians of Philadelphia, 1883.
[5] The American Journal of the Medical Sciences, December, 1897.

interspace over the apex beat, which could be distinctly felt. The point of puncture was about three and one-half inches to the left of the middle line of the sternum, under the left mammary gland, and perhaps through its lower edge. The Roberts pericardial trocar was employed, and worked satisfactorily, the vacuum of the aspirating pump being attached after a little fluid had flowed from the trocar. The introduction of the needle, which was made without attaching the aspirator, was followed by pushing forward the internal cannula. The trocar was introduced to a depth of about 3½ cm. The point gave the impression of being within a cavity, and the beat of the heart against it was easily felt. The external portion of the trocar oscillated with the cardiac pulsations. Three ounces of a very bloody serum were drawn off. That this was not pure blood was shown by the lightish color and the yellowish-red stain made on the towels when some drops soiled them. In order to make a strong vacuum, after the small bottle was about half-filled, the aspirating apparatus was detached. The contents of the bottle had coagulated so promptly that it took a little time to wash out the bottle and to obtain some of the fluid in sterile test-tubes for bacteriological examination. The aspirator was attached to the trocar again, but no further fluid was obtained. When the aspirating apparatus was detached there was a rush of air into the bottle, showing that a vacuum had been properly obtained. No air flowed into the chest, as the trocar on being withdrawn was found to be plugged with a clot of bloody lymph.

The wound was sealed with collodion and cotton. I thought it not wise to withdraw the inner cannula to remove any possible plug, because this would have left the sharp point of the needle exposed and liable to lacerate the heart wall.

Percussion over the upper cardiac region after the patient had been tapped showed clearness where previously there had been dulness. The woman, after the operation, seemed to breathe more easily, and had a better pulse. She was somewhat excited during the operation, but did not seem to suffer much real pain. Ethyl chloride was used to freeze the skin before the puncture was made.

Before the operation there was dulness of the right chest posteriorly, with moist rales. There was marked dulness over the heart. The dull area was somewhat irregularly triangular, with the base downward. This dulness extended into the left axillary region. The dull area seemed to be displaced forward when the patient turned on the right side. The cardiac sounds and impulse were quite distinct in front, and a friction sound was heard at the base of the heart. This was said to be less than on the previous day. The cardiac sounds were heard posteriorly. There were some rales posteriorly in the left chest. The patient was breathing very rapidly, and had a weak, frequent pulse, but was able to lie flat on

her back even before operation. The day after operation she was in better condition than on the day of operation, and the cardiac dulness, which had been diminished by operation, was not increased.

On March 12, 1904, at 12.30 P.M., it was determined to make another aspiration, because the pericardial sac had evidently refilled. A puncture was made with the Roberts trocar in the fifth interspace, two and three-quarter inches to the left of the middle line of the sternum. The aspirator pump was attached, but nothing was obtained, except a very few drops of bloody fluid. The trocar was then withdrawn and found to be plugged. A second puncture was then made in the same interspace, three and three-quarter inches from the mid-line of the sternum. The puncture, made a few days previously, had been made, in the interspace above, three and a half inches from the mid-line of the sternum and through the lower portion of the breast gland. The second puncture, made to-day, obtained by aspiration four and one-half fluidounces of dark-bloody fluid. The fluid was much darker than that obtained a few days ago, and did not coagulate so quickly as that did, if it coagulated at all. It was thicker than the previously obtained fluid. The trocar moved with the heart beats in both punctures to-day, but not so vigorously as it did on the former occasion. At the last puncture the trocar was buried in the tissues about 9 cm. The hand of the operator received the impression that the point was in a large cavity. At the first puncture the end seemed not to enter a large cavity, but to strike against some solid body within the chest. An increased resonance was obtained by percussion of the precordial region after the operation. The patient died early the next(?) morning.

The autopsy showed the pericardial cavity nearly free from fluid; the heart was covered with shaggy lymph, particularly about its base, and there were adhesions between the heart and pericardium. The punctures in the chest wall were in the fourth and fifth interspaces, and the first puncture made on the second day scraped or went through the edge of the costal cartilage above the space.

Upon the front of the heart was a small ecchymosis without apparent wound that looked as if it might have been caused by contact with the end of the trocar. This fact could not be definitely confirmed, as the point of ecchymosis was not very marked. There was a considerable amount of fluid in the left pleural cavity, and a condition of pleuropneumonia. There was some congestion and consolidation of the right lung.

CASE II.—Colored man, aged thirty-one years, in the Polyclinic Hospital under Dr. Riesman. Admitted on March 22, 1904; died on March 28, 1904.

On March 24, 1904, at 11 P.M., I found an enlarged area of cardiac dulness, and valvular murmurs present and easily heard. The

apex beat was seen and felt under the left nipple. I did not believe there was much fluid in the pericardium, though the dulness extended to the right of the sternum. Heart was supposed to be enlarged. Some dulness of the right chest existed posteriorly, with some harsh breathing. At the right base posteriorly there was heard what seemed like pleural friction, but I was uncertain whether it was not rales. Left chest posteriorly showed some dulness. The question in my mind was whether the pulmonary congestion was secondary to the heart lesion, or whether the old cardiac valvular disease had the pulmonary condition added to it and was causing weak pulse (130?), rapid respiration, and sweating, and dyspnœa. The man was not sitting up to breathe. I decided that there was not enough fluid in the pericardium to justify tapping. I had not the benefit of Dr. Riesman's presence to aid me in the diagnosis.

Dr. Riesman sent word on March 25th that he thought tapping was desirable, but could not stay to the operation. I saw the patient and found the condition to be about as the day before, but more dulness in the cardiac area appeared to be present. I tapped in the fourth right interspace close to the sternum with Roberts' aspirating trocar, not attached to vacuum until after insertion. Three fluidrachms of slightly reddish fluid were obtained. The trocar did not move with the heart, but with respiration.

I then punctured in the fifth left interspace directly over the apex beat about one and one-half inches below the nipple, as it seemed desirable to be sure there was no large effusion overlooked. The end of the trocar seemed to strike the heart and perhaps to be embedded in the heart muscle, because it moved with such vigor with the heart beats. No fluid, except a few drops of blood, escaped. The pump brought very little fluid, and, after repeated attempts to get fluid, the instrument was withdrawn. Attempts were made to obtain fluid by altering the position of the end of the cannula, but none was obtained. The end did not feel to be free in a cavity of any size. The end of the cannula contained blood clot, and there was a free flow of blood from the wound until it was closed with cotton and collodion. The patient at one time complained of severe pain, and it was then that the operator felt that the heart had been wounded.

The next day the patient seemed better; the pulse was stronger, and it was thought that the area of cardiac dulness on the right of the sternum was less.

Patient died on March 28th. Autopsy showed no pleural effusion; no fluid in pericardium, but marked amount of lymph in pericardium. The heart was greatly hypertrophied. No mark was found of wound of heart, but this would probably have been concealed by lymph deposits.

CANCER OF THE PANCREAS AND GLYCOSURIA.

AN HISTOLOGICAL STUDY OF THE CHANGES IN THE ISLANDS OF LANGERHANS.

By Richard M. Pearce, M.D.,
Director of the Bender Laboratory, Albany, N. Y.

This investigation was undertaken for the purpose of determining what relation, if any, the islands of Langerhans may have to the glycosuria occasionally seen in connection with cancer of the pancreas. That pathological changes in these structures are frequently associated with diabetes has been satisfactorily demonstrated by the investigations of Opie[1] and others, and has led to a more definite knowledge of a form of diabetes which may properly be called pancreatic diabetes. No attempt has been made on the other hand, as far as I am aware, to demonstrate the presence of similar changes in connection with the glycosuria occasionally associated with cancer of the pancreas. That some of these changes —hyaline degeneration, chronic interacinar pancreatitis involving the islands, and, according to a few investigators, diminution in the number of the islands—might result from the involvement of the organ by cancer is evident from our knowledge of the secondary lesions frequently accompanying such invasion. It is well known that duct obstruction, frequently the result of cancer of the head of the pancreas, readily causes a chronic pancreatitis; and it is possible also that the destruction of a large portion of the pancreas parenchyma by the new-growth may destroy the islands to such an extent that they are no longer equal to the demands made upon them.

On the other hand we have no adequate explanation of those cases in which, though the pancreas is extensively or completely replaced by the new-growth, diabetes does not exist. Such complete destruction, as in the cases reported by Litten[2] and v. Hansemann,[3] is analogous to the extirpation experiments by v. Mering and Minkowski,[4] but the absence of glycosuria is opposed to their results. v. Hansemann has attempted to explain the discrepancy by assuming that in primary cancer of the pancreas the tumor cells originating from pancreas parenchyma inherit the function of internal secretion peculiar to the normal cell. This explanation, however, is entirely hypothetical, and in the light of our present knowledge of pancreatic diabetes loses its force unless we assume that all primary cancers of the pancreas arise from the islands of Langerhans, which, despite the recent publication of Fabozzi[5] supporting such origin appears most improbable. If our newer theories concerning the relation of the islands to carbohydrate metabolism

are firmly grounded we would expect to find evidence of the persistence of the islands in such cases. With these various possibilities in mind, I have made a careful histological study of 30 cases of cancer of the pancreas, in 3 of which glycosuria was present.

The literature offers but scanty information concerning the frequency with which glycosuria occurs in connection with cancer of the pancreas. Such cases are not uncommonly reported, but without reference to the frequency of cases not complicated by glycosuria. From a hasty review of the subject I believe the proportion (1 in 10) shown by my cases to be high. We have, however, definite information concerning the reverse condition; that is, the frequency of cancer of the pancreas in connection with all forms of diabetes. In Oser's[6] series of 188 cases of diabetes, cancer occurred in 24; in Williamson's[7] series of 23, once; and in 139 cases reported by Windle,[8] in 3. v. Hansemann's[9] tabulation of 72 cases of diabetes with pancreatic lesion contains 5 cases of cancer. I have examined many of the original descriptions of the cases quoted in these series, with the object of determining if any peculiar macroscopic or microscopic conditions existed. The task has been most unsatisfactory, for many of the reports are of a clinical nature and gross and histological descriptions are meagre or entirely lacking. This analysis, however, confirms the well-known clinical fact that in the majority of cases the new-growth is in the head of the pancreas and by duct obstruction causes an atrophy (chronic pancreatitis?) of the distal portion of the organ. This point is especially emphasized by v. Hansemann, Dieckhoff,[10] and Windle.

The material upon which this study is based consists of the tissues from 30 cases of cancer selected from a group of 35 examples of new-growth in the pancreas. As the material has been gathered from different sources, often from routine collections of autopsy material, it has not always been possible to procure tissues from the different portions of the uninvolved pancreas as well as from the cancerous portion, nor for the same reason have essential data concerning clinical history and pathology been available in all cases.* Thus while all cases have been utilized in the study of the histological changes but 21 have been available, on account of incomplete examination of the urine, in arriving at conclusions concerning the occurrence of glycosuria. The 30 cancers studied may be classified as follows: primary in the head of the pancreas, 9; in other portions of the organ, 4; secondary to gall-bladder or ducts, 5; to stomach, 8; to breast, 1; and to uterus, 1. Glycosuria occurred in but 3 cases, in 2 of which the tumor was primary in

* I take this opportunity to acknowledge my indebtedness to Prof. F. Marchand, of Leipzig; Dr. Ludwig Hektoen, of Chicago; Dr. F. B. Mallory, of Boston; Dr. James Ewing, of New York; Dr. George Blumer, formerly of Albany; Dr. W. G. MacCallum, of Baltimore; Dr. W. T. Longcope, of Philadelphia, and Dr. M. Herzog, of Chicago, who have kindly placed material at my disposal.

the head of the pancreas; concerning the third, no clinical or pathological notes were available.

The results of the histological examination, especially as concerns the islands of Langerhans, are more readily described under the following headings: changes in (*a*) the immediate neighborhood of the new-growth, (*b*) at a distance from the tumor, (*c*) in cases with extensive involvement, but no glycosuria, and (*d*) in cases accompanied by glycosuria.

(*a*) The important changes at the edge of the advancing cancer are the persistence and increase in size of the islands of Langerhans. While the glandular elements are invaded and replaced by the new-growth and the newly formed connective tissue, the islands remain unaltered in the midst of the stroma and occasionally are even enclosed by a mass of tumor cells. Not only is this true of the edge of the tumor, but in well-infiltrated parts, the islands may be seen in the stroma without remnants of acini. The increase in size of some of these structures is four to five times that of the normal islands. These giant islands are typical in structure and readily distinguished from small alveoli of cancer cells. They represent a true hypertrophy of the islands and not altered pancreas acini.

(*b*) The changes at a distance from the tumor depend apparently upon the location and size of the tumor. With a cancer of the head of the pancreas causing pressure upon the duct a chronic interstitial pancreatitis of severe grade always existed, which, with the exception of one case to be described later, was always of the interlobular type. The islands persist in the midst of dense connective tissue and are not invaded by it. This condition has been observed by Opie in several similar cases without glycosuria. A tumor at the head of the pancreas not obstructing the duct does not cause chronic interstitial changes. Small tumors of any portion of the pancreas are unaccompanied by changes in the islands of the normal portion of the organ; on the other hand, if the new-growth is of considerable size, definite hypertrophy of these structures is apparent.

(*c*) But two cases of diffuse involvement of the organ occurred in this series; in neither was glycosuria present. These are, however, not analogous to those discussed by Hansemann, for areas of normal pancreas could be found here and there, lying in the midst of the new-growth. In such areas were large islands several times the normal size.

(*d*) Three cases of cancer of the pancreas accompanied by glycosuria are included in this series. One of these could not be utilized in the present study because of lack of data; the gross description of the pancreas not being available and the histological study incomplete, inasmuch as only the tumor had been preserved and a study of the uninvolved portion of the pancreas was therefore impossible. The second case, a primary cancer of the pancreas involving the head only and accompanied by a slight intermittent glycosuria

with free fat in the stools, showed no changes in the uninvolved portion of the organ. The islands were few in number and the increase in size usually seen in the immediate vicinity of the new-growth was not evident. The third case was one of cancer of the pancreas with advanced chronic pancreatitis of the interacinar type. Sugar had been present in the urine for several months before death. The entire length of the pancreas was 15 cm.; the proximal 5 cm. occupied by the tumor, the remainder of the organ atrophied and indurated. Histological examination revealed a severe grade of chronic pancreatitis with small, scattered groups of more or less altered acini. Within these, smaller strands of connective tissue had penetrated, involving to a varying extent the islands of Langerhans.

While it is impossible to draw any definite conclusions from such a small number of cases these observations are very suggestive and offer some support of the newer ideas concerning the anatomy and physiology of the islands. The persistence of the islands in the midst of the tumor stroma supports the theory of anatomical independence; an independence which I have recently definitely demonstrated by a study of their development.[11] This persistence is analogous to that described by Schlesinger,[12] Opie, Condon,[13] and Pearce[14] in congenital syphilitic pancreatitis, and by Opie in various other sclerotic conditions of the organ. The increase in size of the islands suggests a purposeful enlargement due to increased function, and therefore of the nature of a compensatory hypertrophy. A similar hypertrophy of these structures has been described by Warthin[15] and by Ohlmacher[16] in connection with cancer of the liver, and is considered by them also to be compensatory in nature, compensating, however, for the lost or limited liver function. The livers of my cases have not been available in all instances for histological examination, and I have not therefore been able to arrive at any conclusion concerning the relation of enlarged islands to lesions of that organ. It is possible that a relation of a compensatory nature may exist between the carbohydrate metabolism of the liver and the islands of Langerhans; but the hypertrophy of the latter structures when associated with cancer of the pancreas is, I believe, an attempt to compensate for the function of the lost islands.

The cases of diffuse cancer of the pancreas without glycosuria can be explained only on the supposition that the amount of normal pancreas remaining is sufficient to furnish the secretion necessary to carbohydrate metabolism. v. Mering and Minkowski found in their extirpation experiments that if one-fourth to one-fifth of the pancreas remained, diabetes did not result; a destruction of the pancreas by cancer we may consider analogous to partial extirpation. In both of my cases of diffuse cancer small areas of pancreas containing islands could be found in the midst of the new-

growth in a sufficient amount to correspond to the unextirpated fifth. In this connection the possibility of an accessory pancreas (Thorel,[17] Sweet[18]) or other glands maintaining the balance of function must also be considered. v. Hansemann's explanation of the absence of glycosuria is not applicable unless we assume that all cancers of the pancreas arise from the cells of the islands of Langerhans.

Finally, we have the cases with glycosuria. In one of these a true diabetes existed; in the other an intermittent glycosuria. The first is readily explained by the presence of an interacinar pancreatitis with involvement of the islands, a type of pancreatitis originally described by Opie in connection with diabetes and since observed by many investigators. It therefore appears that while cancer of the head of the organ with duct obstruction may frequently cause a chronic pancreatitis, glycosuria does not result unless the interacinar form with involvement of the islands develops. This naturally brings cancer diabetes into a common relation with pancreatic diabetes in general.

The case of intermittent glycosuria brings up the vexed question of alimentary glycosuria. It is well known that a normal individual may digest without disturbance from 150 to 250 grams of sugar, but that an increase over this amount may lead to temporary excretion of glucose in the urine. This excretion due to hyperglycæmia is the inevitable result of a sudden flooding of the circulation with an amount of glucose beyond that which the body is able at once to consume. On the other hand, in a number of abnormal conditions where there is no actual diabetes, an alimentary glycosuria may be produced by an amount of sugar which in the economy of the normal individual is easily consumed. Among the prominent conditions in which this occurs may be mentioned neuroses, traumatic or otherwise, organic nervous diseases, alcoholism, infectious diseases, exophthalmic goitre, hepatic and pancreatic disease. Is it not possible that this temporary excretion of sugar is due to some transient disturbance of the function of the islands brought about by vascular disturbances of the islands or by some toxic substance, perhaps of the nature of an autotoxin, affecting the secretion of these structures or temporarily throwing them out of function? In a destructive disease of the pancreas, as cancer, a certain number of the islands are necessarily destroyed; the remainder, however, may be sufficient under normal circumstances to furnish the necessary secretion, whatever it may be, essential to carbohydrate metabolism; but if overtaxed by an unusual injection of glucose, hyperglycæmia and a consequent glycosuria might result. This explanation has occurred to me in connection with my case of cancer accompanied by intermittent glycosuria; and that it is not entirely hypothetical is indicated by the observations of Ssobolew,[19] confirmed by Herzog,[20] that in some cases of permanent diabetes the

pancreas exhibits a great diminution in the number of islands and in some cases an entire disappearance. This deficiency, however, is far from proven, and in mentioning it I do not wish to be placed in the position of advocating a pancreatic origin for all forms of diabetes.

CONCLUSIONS.—We have a definite basis for ascribing a certain portion of the cases of diabetes to lesions of the pancreas and ultimately to lesions of the islands of Langerhans. As a result of the study here briefly outlined we can, I believe, include the permanent diabetes of cancer of the pancreas in this group. Further observation must be made before the intermittent glycosuria can be attributed to destruction of large numbers of islands. The absence of diabetes in cases of extensive involvement of the pancreas would appear to be due to the survival of small fragments of pancreas, including a number of islands sufficient to carry on their peculiar function. The persistence of the islands under the adverse conditions described supports the observations heretofore made concerning their anatomical independence, while their enlargement, suggesting as it does a compensatory hypertrophy, is corroborative of the theory that they have an independent special function.

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ASCARIDES IN THE BILE-DUCTS SIMULATING GALLSTONE SEIZURES.

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Intestinal worms are not considered common causes of biliary colic; they are, perhaps, not sufficiently considered in this role, for when we remember that the natural habitat of these parasites is the small intestine, and that not infrequently do they pass into the common duct and there effectually occlude the lumen of that canal and completely obstruct the flow of bile, it is obvious that their presence would give rise, quite naturally, to the complex chain of symptoms noted in the occlusion of that duct from other causes.

Where the natural current of normal bile is not interfered with it is a sterile fluid. This has been proven experimentally on dogs by Netter[1] and confirmed by Gilbert and Girade,[2] and further confirmed by Naunyn,[3] who reports a case wherein the bile was sterile two hours after death.

Bile has also been regarded an antiseptic, and to this property has been ascribed the function of preventing decomposition during digestion; but this premise has failed to receive sufficient proof, while on the other hand it has been proven that it does not possess any antiseptic properties. In the report of a case of biliary fistula Mayo-Robson observed that the absence of bile from the intestine for a period of fifteen months did not lead to any irregular fermentation processes, and concludes "that the alleged antiseptic effect of bile on the feces is probably imaginary."[4] Professor Birch has reached the same conclusion[5] after numerous cultivation experiments.

So much, then, in consideration of normal bile when its natural current is not impeded.

In emphatic contrast to the researches noted above we know, from equally able investigators, that when the flow of bile along the ducts is for any reason arrested, micro-organisms *usually do* invade the gall-bladder, on the hypothesis that they gain entrance either from the blood or from the intestines.

Charcot and Gombault[6] were the first to demonstrate this fact by ligating the common duct in dogs; later this was confirmed by Netter,[7] who, after an aseptic ligature of the common duct in dogs, found that both staphylococcus and bacillus coli commune could be cultivated from the stagnant bile. Bouchard[8] cultivated the bacillus coli commune from the bile of cases suffering with disease of the biliary tract which was of sufficient severity to produce inflammatory changes on the mucous lining of the ducts, thus oblit-

erating the lumen of the canal, and in consequence producing a stagnation of the bile.

In answer to the query, "How do these bacteria reach the gall-bladder?" Mayo-Robson[9] gives three possible sources, viz.: (*a*) through the bile-ducts, or (*b*) from the blood, or (*c*) directly through the wall of the gall-bladder.

It is, then, only in diseased conditions that these micro-organisms are present in bile, and it seems that the biliary apparatus will tolerate a moderate degree of inflammatory involvement and be perfectly able to maintain its integrity, providing the flow of bile is not interfered with, but cannot withstand the closure of the chief duct and resist the invasion of the bacteria.

This fact, then, becomes the pivotal point which must determine the causes of gall-bladder infections. It makes no difference whether the bile current is stagnated by an inflammatory process involving the duct to the degree of occluding its patency, or whether there is an impacted gallstone in the common duct, or whether an ascaris has wandered from its habitat and entered the common duct, or the simple aseptic ligature, experimentally performed; the result is the same, the flow of normal bile is prohibited, and bacterial invasion is certain to be a consequence.

It is not surprising, then, that the case cited below was admitted to the hospital and the opinion given of probable impacted gall-stone in the common duct:

A. S., aged thirty-four years, Austro-Hungarian. Engaged in railroad grade work. Lives in a temporary camp with other men of his class. Surroundings very unhygienic. Food improperly prepared and of poor quality.

April 12, 1904. *Present History.* Complains of pain in stomach, no appetite, tongue coated and foul, fetid breath. Has had attacks of severe colic, lasting a few hours, leaving a sense of soreness in epigastrium. Temperature, 99° F.; pulse, 80; anxious facial expression.

19*th.* Admitted to Mercy Hospital. Deeply jaundiced; mucous membranes of the mouth and conjunctiva yellow; sclerotic membranes of both eyes deeply jaundiced. Hepatic area of dulness much increased, border of liver extending 6 cm. below costal arch; exceedingly tender on slight pressure over site of gall-bladder, tumor evident between the costal margin of ninth rib and umbilicus. Pulse, 60° F.; temperature, 98.4; respiration 16. Frontal headache, anorexia, and eructations of gas. Constipated. Urine: dark-brown colored; specific gravity, 1028; reaction, acid; chlorides, 16 per cent.; phosphates, 8 per cent.; sulphates, 8 per cent.; albumin, none; sugar, none. Biliary pigments distinct by Ulzmann's test. Biliary acids were detected by Dr. Oliver's test,[10] and estimated by his standard table as follows: To 4 c.c. of Oliver's solution 1.25 c.c. of urine was added; a very distinct milkiness appeared at once.

In the second trial 4 c.c. of the test solution was added to 1 c.c. of urine, with prompt milkiness. In the third trial 4 c.c. of the test solution was added to 0.60 c.c. of urine, resulting in no immediate reaction, but in a short time slight milkiness occurred. According to Oliver's table of standards this would indicate a percentage increase of 600. Stool almost white, and about the consistency of putty.

Patient was ordered a liquid diet, and, as was suggested by Mayo-Robson,[11] he was given calcii chloridi, 2 grams three times daily, to lessen the tendency to hemorrhage during the operation. Calomel 0.65 every hour for three doses, follow at once with $MgSO_4$, 15 grams in half-glass of hot water.

20th. Pulse, 49; temperature, 97° F.; respirations, 16. No bowel movements. Urinated about 300 c.c. during the night, highly colored. Pain quite severe in stomach. Deep jaundice; headache. Calomel 0.65 every hour for three doses, follow at once with $MgSO_4$, 15 grams in hot water. Calcii chloridi, 2 grams three times daily.

21st. Pulse, 58; temperature, 97.8° F.; respirations, 16. Bowels have not moved; urinated four times. Complains of headache. Deeply jaundiced. Pain constant. Calomel reordered as above, followed by $MgSO_4$. Calcii chloridi continued. Prepared for operation.

23d. Pulse, 52; temperature, 98.2° F.; respirations, 16. No breakfast. Had four bowel movements, clay colored, thin and offensive; the second movement occurred at 5 A.M., and was allowed to remain in the bed-pan and placed in the closet. The nurse reported a long, brown body in the evacuation, and Dr. J. M. Crowley, the assistant superintendent of the hospital, examined the evacuation and secured a live ascaris lumbricoides 28 cm. long. On my arrival at the hospital, Dr. Crowley and I examined the evacuation for the ovæ, but none were found. It was thought that possibly this worm was responsible for the symptoms manifested, and operation was postponed. Santonini, 0.65, with calomel, 1.95, was ordered at noon, to be repeated at 9 P.M., and followed by Ol. ricini 30 c.c. in the morning.

24th. Slept well. Bowels moved four times freely, clay colored, thin; urine dark. Deeply jaundiced.

The subsequent history is not of especial interest. In a few days the pain subsided, the liver area of dulness became normal, no pain on pressure could be elicited, tongue cleaned, appetite returned, jaundice gradually faded, and he was discharged May 5, 1904.

It might be of interest to note that, while the patient began to improve in every way and the appetite was fully restored, while the bowels moved regularly every day, it was not until the day previous to his discharge from the hospital that the feces resumed their natural color, and when the coloring of the bile did appear in

the stools it was not gradual but spontaneous; the evacuation preceding the one of natural color was as cream colored as they were when he first entered the hospital.

Mertens[12] has reported forty-eight cases of ascarides in the bile-ducts, but in only five cases were the symptoms such as would suggest the presence of gallstones, and in but two of these was the cause determined during life.

In his own case, a woman of thirty years of age was admitted to a hospital following the third attack of biliary colic, which began with pain in the gall-bladder region, associated with vomiting, and followed by deep jaundice; both liver and spleen were increased in size. The patient rapidly became emaciated for seven weeks, at the end of which time she passed two partially macerated round worms, and she rapidly improved and ultimately recovered.

When we consider that these worms inhabit the upper portion of the small intestine, and recall the migratory nature of the parasite, the wonder is not that they occasionally wander into the common duct, but that they are not found there more frequently than observers would lead us to believe.

Their presence in the bile-duct certainly interferes with the normal flow of the bile and invites bacterial invasion by stagnation of that fluid, and I believe that in the cases cited above such an infection occurred, and this premise is substantiated by the tardy appearance of the bile in the stools. There is no doubt but that the gall-bladder and the bile-ducts were infected and suffered inflammatory hypertrophy sufficient to completely obliterate the lumen of the common duct, and even after the removal of the provoking cause were slow to repair this damage and functionate normally. The pain symptom further emphasizes the truth of this statement.

Kehr[13] states that pain in gallstone disease is not due, as is commonly supposed, to the pressure of a hard substance held in a soft mucous-membrane tract, either in the cyst or the ducts; the mere presence of stone in these passages may interfere with the normal currents of the bile, and that bacterial invasion which follows this impeded current invade the gall-bladder and its ducts. The result of this inflammation is the softening of the mucous membrane of the gall-bladder and the ducts, and the transudation of serous or purulent fluid into these hollow organs; at first the transudation takes place by reason of the increased circulation attracted to this site by the bacterial invasion of the coats of either the gall-bladder or the ducts, and when first poured out is a serous fluid; later, as the bacterial invasion increases, this serous fluid is readily converted into a purulent fluid.

In either case the gall-bladder and its appendages are distended, and the nerve endings throughout its surface are put upon the stretch and dragged upon, and this gives the symptoms of pain, and is solely excited by the distention of the walls of the gall-bladder and ducts.

It is not the character of the fluid in those hollow organs that determines the pain, but the fact that *any* fluid has produced distention sufficient to violate the nerve endings.

Kehr[14] mentions a simple interesting experiment in proof of this statement: following an operation on the gall-bladder where there is a fistula established, inject into the gall-bladder physiological salt solution; the moment distention occurs, complaint will be made by the patient of severe cramp in the stomach.

The jaundice of the case was very pronounced; all visible tissues were deeply stained; the skin was dry and harsh. This color appeared quite abruptly, following shortly after my first examination on April 12th, and was of the same deep color that was so characteristic a feature until the passage of the worm on April 23d; after this the color gradually faded.

It seems that these round worms are very commonly found in autopsies upon laborers of this class, especially among the Italian. Dr. F. F. Agnew, formerly of Blockley Hospital, Philadelphia, stated to me in a conversation recently that in a number of autopsies during his service he cannot recall an instance when these worms were not found in this class of laborers. Thus it would seem that the mode of living and the sanitary surroundings had a determining influence.

The hospital record shows that this patient complained bitterly of pain, and was not able to sleep well from the date of his admission, April 19th, until the date on which he passed the worm, April 23d. After that date his appetite improved and he slept well, and when seen he would make deep pressure over the former site of his pain, which was a little to the right of the epigastric median line, and say in English, "No pain," and shake his head vigorously to emphasize the statement.

There were no special symptoms that might lead one to suspect the presence of ascarides; the clinical picture was purely one of biliary colic, and, combined with the quickly developing jaundice and the continued pain, presented a typical case of obstruction of bile from whatever cause.

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ACUTE PRIMARY CHOLECYSTITIS, WITH A REPORT OF FOUR CASES.

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Potain,[1] in 1882, and Courvoisier,[2] in 1890, described acute cholecystitis as a rare but rapidly fatal disease. In 1898 Richardson[3] published an article that should have convinced every practitioner that acute inflammation of the gall-bladder occurs not only as a complication of gallstones, or secondary to other diseases, but also as a primary and serious affection characterized by signs and symptoms that correspond to the extent and intensity of the pathological changes. I believe that most medical men are rather doubtful as to the occurrence of acute primary cholecystitis, and many still believe in such statements as the following: "Acute empyema, or gangrene of the gall-bladder, is associated with gallstones in 74 per cent. of the cases. In the remainder it occurs in zymotic diseases, as typhus fever, variola,"[4] etc. The time has come when we should discard such statements. We should know that acute primary cholecystitis does occur, that it can be diagnosticated, and that in most cases it can be treated successfully.

In this paper I shall discuss only cases of acute inflammation of the gall-bladder in which gallstones were not found, and in which the condition could not be considered secondary to any other disease.

Case I. *Sudden onset; chill; biliary colic; history of two primary attacks; operation; cholecystitis found; many adhesions; no gallstones; chronic appendicitis; recovery.*—Joseph B., a miner aged twenty-nine years, was seized with a violent chill. This occurred about midnight. Shortly afterward he began to suffer from violent paroxysmal pain in the abdomen. He vomited and the pain disappeared. In a few minutes the colic returned. The pain was very severe, was most intense in the pit of the stomach, and radiated to the right scapular region. Between midnight and 4 a.m. he had six paroxysms of pain. Examination (4 a.m., June 16, 1901) was as follows: The patient was in shock. Pulse rate, 110. There was no fever. His tongue was coated. The pupils were slightly dilated, but reacted normally. There was no jaundice. Examination of the heart and lungs was negative. The abdomen was slightly distended and was tender. The region of the gall-bladder was extremely tender. The right rectus was more tense than was the left. The remainder of the examination was negative. I washed out his stomach and gave him three-eighths of a grain of morphine and one-one-hundred-and-fiftieth of a grain of atropine hypodermically.

Previous History. The patient had measles when a child. He had never suffered from typhoid, variola, or pneumonia. Two years previously he was ill for one week with an attack similar to the present sickness. During this illness the pains were very severe, and he thought he had fever. Eight months ago he suffered from an illness that confined him to his bed for two weeks. The pain at this time was severe, and was paroxysmal for five days. Then it became continuous and gradually subsided at the end of two weeks. The region of the gall-bladder was tender for four weeks following this illness. The patient had never been jaundiced.

Operation. The morphine gave very little relief. The paroxysms of pain continued. At 8 A.M. his temperature was 101°, and his pulse rate 110. The patient was etherized at 9 A.M. After anæsthesia was complete I was unable to feel the gall-bladder or to determine that the liver was enlarged. An incision was made along the outer border of the right rectus muscle, extending from the costal arch downward. The omentum, colon, and gall-bladder were firmly matted together. I freed the gall-bladder and found that it was slightly enlarged, was very tense, and of a very dark color. I then brought the appendix into the wound. It showed evidences of chronic inflammation. After removing the appendix the gall-bladder was surrounded with gauze, aspirated, sutured to the transversalis fascia, and opened. It contained very dark and thick bile. The mucosa of the gall-bladder was œdematous and injected. No gallstones were found.

The patient made an uneventful recovery. The drainage was profuse, but contained no stones. The temperature and pulse rate became normal on the fourth day. The fistula was closed at the end of six weeks, and the patient has been well since that time.

A smear from the gall-bladder contents showed the presence of a short bacillus that stained well with methylene blue.

CASE II. *Chill; colic; high temperature and pulse rate; local tenderness over the gall-bladder; operation; gall-bladder enlarged, tense, and showed beginning gangrene in one place; cholecystostomy; no stones found; recovery.*—George T., aged twenty-four years, was seized suddenly with severe abdominal pain. The pain was paroxysmal, was located in the epigastrium, and did not radiate. He vomited twice. He had a severe chill, but cannot remember when this occurred. He is of the opinion that the chill preceded the pain. I saw him, with Dr. B. B. Slick, of Ridgway, Colorado, twelve hours after the onset of his trouble. At this time his temperature was 104° and his pulse rate 146. The pain had ceased. The region of the gall-bladder was sensitive on deep pressure. The right rectus muscle was rigid. The gall-bladder could not be palpated. Dr. Slick told me that the paroxysms of pain were very severe for ten hours and that one-quarter of a grain of morphine

hypodermically had no effect on them. The patient's previous history showed that he had never been sick before.

Operation. Local anæsthesia was used. The gall-bladder was exposed through a vertical incision. It was enlarged and distended. The fundus showed an area of beginning gangrene. The gall-bladder was aspirated, sutured to the transversalis fascia, and opened. The organ was sufficiently enlarged so that it could be brought far enough into the wound to suture beyond the gangrenous area. The gall-bladder contained dark, thick material.

The patient made a rapid recovery.

No bacteriological examinations were made.

CASE III. *Chill; colic; fever; local tenderness; vomiting; operation; gall-bladder not perforated; general peritonitis; gangrenous cholecystitis; no gallstones; death.*—Mrs. S., aged thirty-six years, complained of violent abdominal pain about 11 P.M. At about the same time she had a violent chill. She vomited several times. The pain was paroxysmal, was located in the pit of the stomach, and did not radiate. She was given one-quarter of a grain of morphine hypodermically every hour. One and one-quarter grains were given before she was relieved. She then slept for six hours. When she awoke the pain returned, but was less severe. After the first thirty-six hours the paroxysms of pain ceased and she complained only of a dull, continuous pain. She ceased vomiting at the end of twenty-four hours, and did not begin to vomit again until the sixty-fourth hour. The bowels moved on the second day in response to five grains of calomel and an enema. The temperature ran from 101° to 103°; the pulse rate from 110 to 120. There was no jaundice. She had rheumatism fourteen years ago, and for eight years had suffered dyspnœa after exertion. For five years she had suffered more or less from the pain and hemorrhage caused by a uterine fibroid. She had had no acute infectious diseases.

I saw the patient seventy-two hours after the beginning of the illness. At this time the temperature was 104° and the pulse rate 130. The abdomen was distended, rigid, tympanitic, and tender. The region of the gall-bladder was more sensitive than the remainder of the abdomen. Examination of the lungs was negative. The heart was enlarged transversely. A systolic murmur was present over the apex and in the axilla. There was a leukocytosis of 22,000. The urine was scanty and contained much albumin. The liver dulness was slightly increased in size.

Operation. A longitudinal incision was made over the gall-bladder. The liver was enlarged. The gall-bladder was somewhat enlarged and distended. It was very dark in color, but was not gangrenous or perforated. There were no adhesions. General suppurative peritonitis was present. The appendix was normal. No tumor was felt in the region of the pancreas. The gall-bladder was aspirated and found to contain pus. A rubber tube

and strips of gauze were placed through the posterior abdominal wall, on the right side, to drain the peritoneal cavity. Then the gall-bladder was anchored and opened. No stones were found. The patient died from general peritonitis forty-eight hours after the operation was performed.

Autopsy. General suppurative peritonitis; acute cholecystitis and cholangitis; fibrous myocarditis, with fatty degeneration; parenchymatous degeneration of the spleen, liver, and kidneys; a moderate degree of chronic interstitial nephritis. Atheromatous areas were present in the aorta and in the coronary arteries. There was a fibroid involving the fundus of the uterus.

Case IV. *Acute primary cholecystitis; gangrene of the gall-bladder, with perforation; general peritonitis; death; no gallstones found at operation or autopsy.*—Carl H., a brakeman, aged twenty-seven years, who had had no previous sickness, was suddenly taken ill with a chill and with violent paroxysmal pains in the abdomen. The pain radiated, at times, to the right scapular region. He vomited continuously. His temperature averaged 103° and his pulse rate 120. A small bowel movement was obtained about thirty-six hours after the onset of the disease. On the second day of his illness the pain became continuous. There was no jaundice. There was marked tenderness over the region of the gall-bladder. The abdomen was distended, tender, and rigid.

Operation, fifty-five hours after the beginning of the illness, showed a gangrenous and perforated gall-bladder, with general suppurative peritonitis. The appendix and pancreas showed no marked changes. The patient died thirty hours after the operation. No gallstones were found at operation or autopsy.

Case V.—M. Richardson[3] reports a case of acute cholecystitis occurring in a man, aged forty years, whose only previous illness had been an attack of "inflammation of the stomach," five years previously. The patient complained of acute pain in the abdomen. Twelve hours afterward his temperature was 101°. The abdomen was rigid and was diffusely tender. These symptoms were most marked on the right side. Operation revealed acute cholecystitis. A cholecystostomy was done and the patient recovered. The colon bacillus was found in the gall-bladder.

Case VI. (Reported by Richardson.[3])—A man, aged twenty-eight years, who had never been sick, complained of paroxysmal pains in the groins. A hypodermic of morphine did not give him relief. The temperature was 102° and the pulse rate 108. A laparotomy revealed a general peritonitis. The gall-bladder was gangrenous, but was not perforated. No gallstones were found. The patient died on the fourth day following the operation.

Case VII. (Reported by Richardson.[3])—A man, aged fifty-six years, who had previously had some pain in the region of the gall-bladder, was suddenly taken ill with abdominal pain, vomiting,

fever. Temperature 103° and pulse rate 100. The area over the gall-bladder was markedly tender. In this case the patient had accurately located the point of greatest tenderness without advice or suggestions. Cholecystostomy revealed acute cholecystitis. The gall-bladder contained bacilli and cocci. No gallstones were found. The patient recovered.

Case VIII.—W. A. Lane[5] reports a case of acute primary cholecystitis occurring in a man, aged fifty-four years, who had always been in perfect health. The patient was suddenly seized with severe paroxysmal abdominal pain, prostration, and constipation. Attempts to produce evacuation of the bowels were tried for three days, but were unsuccessful. Laparotomy showed the duodenum and a portion of the colon covered with a layer of lymph. The gall-bladder was much distended, but was not gangrenous or perforated. A cholecystostomy was done. The gall-bladder contained mucopus but no stones. The patient made a perfect recovery.

Case IX.—E. M. Pond[6] reports a case of acute primary cholecystitis occurring in a healthy man aged sixty-five years. The onset was sudden, the pain paroxysmal, and the abdomen very rigid and tender. The area over the gall-bladder was extremely tender. Operation revealed a gangrenous and perforated gall-bladder; general peritonitis; no gallstones. The gangrenous portion of the gall-bladder was removed and drainage employed. The patient recovered.

Case X.—A. J. Ochsner[7] reports a case of cholecystitis occurring in a woman aged fifty-two years. She was sick one week previous to being operated upon. During this time she had four attacks of severe pain in the epigastrium. The gall-bladder was found greatly distended with thick, dark bile. No gallstones were found. A cholecystostomy was done and the patient recovered.

Case XI.—Curtis[8] reports a case of acute fatal peritonitis in which operation revealed advanced cholecystitis without perforation as the cause. The presence of gallstones was not mentioned.

Occurrence. Acute primary cholecystitis is not such a rare condition as is generally supposed. Musser[9] states that the primary form of acute cholecystitis is more common than is usually thought. M. Richardson states that acute cholecystitis, without known pre-existing gall-bladder disease, is more common than intestinal obstruction. The reports of large numbers of cases of operations on the biliary apparatus show plainly that cholecystitis —acute, chronic, with and without gallstones—is not an uncommon disease. But these reports are of little value in determining the relative frequency of occurrence of the acute primary form. The experience of any man who does a large amount of surgery and little else does not give a fair estimate of the relative frequency of occurrence of diseases like acute primary cholecystitis, for the

following reasons: The large majority of the patients, coming to the surgeon of large experience, have first passed through the hands of the general practitioner. Many of these cases are chronic. But the rule is that, although the general practitioner may not have made a diagnosis, he is usually reasonably certain that the case is a surgical one before he refers it to the "surgical specialist." The chronic sufferers may find their own way to the surgeon of large experience, but in the great majority of cases it is the general practitioner who directs the plan of procedure in the acute serious diseases. For these reasons, the man who does very little outside of operative work is at a disadvantage in regard to diseases like acute primary cholecystitis. It is impossible, at the present time, to determine the frequency of occurrence of acute primary cholecystitis. I am of the opinion that acute and subacute primary cholecystitis is much more common than any of us would believe.

Etiology. I am unable to make any positive statements in regard to the etiology. It is probable that the colon bacillus is most frequently the cause of the inflammation. It is possible that the typhoid bacillus may remain latent in the gall-bladder for a number of years and then cause an acute attack of cholecystitis. Hunner[15] reports such a case. These patients usually give a history of a previous attack of typhoid fever. However, Cushing[11] reports one case of gallstones, with acute typhoid cholecystitis, in which there was no history of a previous attack of typhoid.

It has not been positively determined how the micro-organisms reach the gall-bladder. It is generally believed that they come from the intestinal tract. The usual idea has been that they reached the gall-bladder through the common and cystic ducts. Cushing[12] states that in cholecystitis following typhoid the organisms get into the gall-bladder by way of the portal vein. I have thought that the mechanism of infection might be as follows:

When the colon bacillus finds its way into the portal vein it seldom passes beyond the liver. Many times it is excreted in the bile. Now some of these organisms, in being excreted from the liver, might be carried by the bile into the gall-bladder. Some of the organisms might lodge between the mucous folds of the cystic duct and excite an inflammation. The swelling of the lining of the duct would soon close the outlet of the gall-bladder. This would lower the resistance of the gall-bladder mucosa (Charco and Gombault[13] and Netter[14]), and, according to Leubuscher, do away with the antiseptic properties of the bile in the gall-bladder. (Cushing says that the bile is not only not antiseptic, but is a good culture medium.) If we accept the foregoing as the process by which the inflammation starts, we can easily see how distention, gangrene, and perforation of the gall-bladder, and peritonitis, with or without perforation, might occur, according to the virulence of the infection and the resistance of the patient.

PATHOLOGY. I can add nothing to the pathology that has not been given in the report of the cases. It would seem that the presence of pus in the gall-bladder occurs only after the disease has become well advanced, that gangrene of the gall-bladder usually begins at the fundus, and that a virulent peritonitis can and does occur without perforation of the gall-bladder (Robson).

The changes in the liver are comparatively slight. This seems reasonable if we accept the mechanism of the infection as described in the foregoing. The organisms would be prevented from attacking the common and the hepatic ducts on account of the smoothness of their linings and the flow of bile, while the stagnation of the bile and the presence of large folds in the mucosa would predispose the cystic duct to infection.

The general changes in the body correspond to those that accompany any acute inflammatory process.

SYMPTOMATOLOGY. The number of cases of acute primary cholecystitis is too small to outline a definite symptomatology. I shall discuss the symptoms in the order that I believe they occur, and, at the same time, shall mention the relation of the symptoms to the pathological changes.

Chill. The chill may be severe, moderate, or absent. It can be expected in the most severe cases.

Pain. The pain may accompany, precede, or follow the chill. It is of sudden onset, is very severe, is paroxysmal at the beginning, and is located in the epigastrium. It frequently radiates to the right scapular region, and in one of Richardson's cases was situated as low as the groins. The pain, in some cases, is identical with biliary colic. It is doubtless due to the gall-bladder trying to empty itself. When the musculature of the gall-bladder exhausts itself the pain ceases, only to return in a short time. When the tension in the gall-bladder becomes great and its musculature exhausted, the pain becomes continuous. When gangrene of the gall-bladder occurs the pain ceases. I shall not discuss the mechanism of acute colicky pain in the region of the gall-bladder. There are so many contradictory and radical statements on this point, made without proof, that it is impossible to draw conclusions.

Vomiting. Vomiting may be expected in most severe cases. It is an early symptom. It usually ceases after the first twenty hours, but returns if peritonitis develops. No cases of fecal vomiting have been recorded.

Fever and Elevation of Pulse Rate. These are present in all cases. They occur shortly after the patient has recovered from the chill and the shock of the primary paroxysm. The intensity of these symptoms depends on the severity of the infection. They still are present after the gangrene has abolished pain and obscured local tenderness.

Local Tenderness. This is an early and constant symptom. The entire abdomen may be sensitive, but the rigidity and tenderness

are most marked on the right side, and the point over the gall-bladder is most sensitive to pressure, except when the gall-bladder becomes gangrenous. A gangrenous gall-bladder is insensible.

Jaundice is not a symptom of cholecystitis. It may occur as a complication or as part of a pre-existing disease.

Enlargement of the gall-bladder and the liver usually cannot be determined.

Constipation. Constipation is usually present, but in most cases will yield to treatment.

The changes in the blood and urine correspond to those found in ordinary acute infections.

Diagnosis. Cholecystitis is recognized by the sudden onset, the characteristic pain, the fever, and the local point of tenderness. Gangrene of the gall-bladder is strongly suspected when the pain and tenderness cease, or are markedly diminished, with the general symptoms increasing in severity. Collapse might follow perforation. Further reports will be necessary to determine this point. It is impossible to recognize gallstones when they have given no previous symptoms.

Prognosis. Acute primary cholecystitis is amenable to successful surgical treatment in all cases in which operative treatment has not been unduly delayed. The mortality depends entirely upon the promptness of recognition and treatment. I am of the opinion that most of the cases would die if not treated surgically. Doubtless many patients who have died from "inflammation of the bowels" had acute primary cholecystitis at the beginning of their illness.

The subacute and the mild cases of acute primary cholecystitis recover. I believe that primary cholecystitis may occur in all degrees of severity, from the mild attacks that Musser believes to be followed by gallstones to the most severe ones that cause death in twenty-four to forty-eight hours.

Treatment. I know of no medical treatment for cholecystitis. If the patient refuses surgical aid, the stomach should be washed out, rectal feeding resorted to, morphine given if necessary, and cathartics avoided.

I am of the opinion that the advice of Ochsner not to operate during an acute attack of cholecystitis is dangerous. I believe that all acute cases should be operated upon as soon as the diagnosis is made. Cholecystostomy meets the indication in the early stages and is not so severe on the patient as is cholecystectomy. At present I should advise removal of the gall-bladder only in cases with extensive gangrene, and drainage of the gall-bladder in all other acute cases. The presence of stones does not modify the treatment. I believe that in acute infected cases cholecystostomy has a smaller mortality than has cholecystectomy. If the foregoing advice is followed, a secondary operation may occasionally be required.

This is not especially objectionable. Secondary operations on the gall-bladder are usually safe and are not complicated with acute infection.

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VARIETIES OF SPLENIC ANÆMIA.

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THIS report of five cases, with pathological studies in three of of them, is presented as a contribution to the knowledge of the condition generally designated as splenic anæmia. I have elsewhere expressed doubt regarding the individuality of such a condition, and the conviction that many different sorts of diseases have been classed under this name. For convenience of clinical terminology the name may, however, be retained, and perhaps some order may be established before long.

CASE I. *Male, aged fifty-nine years, history of dysentery(?), duration over two years, probably six years or more; stunted growth, pigmented skin, clubbed fingers, osteoarthritis, enlarged spleen; chloroanæmia with leukopenia, hemorrhages, diarrhœa; early enlargement followed by diminution in the size of the liver; numerous intercurrent infections; death in stupor; autopsy.*—L. C., a cigarmaker, aged fifty-nine years, native of Belgium, was admitted April 18, 1900. The history recorded at that time is as follows: His father died of phthisis, his mother of jaundice, one brother of rheumatism. He had jaundice twenty-two years before and gonorrhœa sixteen years before. He denied syphilis and malaria, but had been in Mexico and Africa with the French army and may have had malaria. He gave an uncertain account of some sort of diarrhœal

disease in Africa, perhaps dysentery. He was married at thirty-two; his wife and two children died of phthisis.

Four and a half years ago noticed a beginning alteration in the skin in the form of patches of pigmentation, alternating with light areas. Six or seven months ago had a chill and fever, and this has been repeated at intervals of a few weeks. He complains of a buzzing in his ears and of a scaly, itchy eruption on his legs. During the last two months has grown weak and dyspnœic.

FIG. 1.

Status Præsens. The patient is a somewhat undersized man. There is a bronze discoloration of legs and arms, and to a less extent of abdomen and chest, with areas of lighter color between. In places on the abdomen the skin in the bronzed areas is desquamating, leaving normal-colored skin beneath. The fingers are markedly clubbed. Patches of dermatitis are found on both ankles, and there

is slight œdema. The liver extends from the fifth rib to within an inch of the umbilical level. The spleen extends from the eighth rib to an inch below the anterior superior spine of the ilium. Two marked notches can be felt in the anterior border. Scattered rales are heard in the lungs; a systolic murmur and an accentuated second sound at the aortic interspace. Otherwise normal physical signs are obtained (Figs. 1 and 2).

FIG. 2.

April 18, 1900. Blood examination: Red blood corpuscles, 3,520,000; hæmoglobin, 51 per cent.; white blood corpuscles, 5280.

May 1*st* Blood examination: Red blood corpuscles, 3,630,000; hæmoglobin, 76 per cent.; white blood corpuscles, 2600. (The

first hæmoglobin estimate was thought erroneous at the time.) Differential count: Polymorphonuclear, 68.9 per cent.; mononuclear, 1.9 per cent.; transitional, 4.9 per cent.; lymphocytes, 22.6 per cent.; eosinophiles, 1.4 per cent.

Urine Examination. Specific gravity, 1010; acid; no albumin; no sugar; microscopically negative.

6th. The patient had a chill, followed by fever, delirium, and cellulitis of right leg, which finally required incision for the removal of a small amount of pus. The leukocytes numbered 6120; the blood was examined for malarial organisms at the time of this chill, and repeatedly later, but none were found. The cellulitis seemed the result of scratching one of the eczematous patches on the ankle.

June 5th. Slight jaundice, no change in liver, no fever.

13th. Right-sided orchitis; œdema of right leg.

14th. Chill; temperature, $104\frac{3}{5}°$; impairment and rales at right base.

21st. Still impairment at right base.

24th. Blood: Red blood corpuscles, 3,560,000; hæmoglobin, 46 per cent.; white blood corpuscles, 2760.

July 3d. Considerable hemorrhage for several days, due to extraction of a tooth.

August 9th. Continuance of slight jaundice; also occasional elevations of temperature. No bile in urine.

September 11th. Marked pharyngitis.

October 17th. Periodic neuralgia in various parts of the body of late.

November 2d. Spleen seems a little smaller; liver certainly smaller.

9th. Definite neuritis. Arsenical treatment suspended. Improvement on discontinuing the drug. Pigmentation more marked of late.

26th. Another attack of lymphangitis of right leg. Inguinal glands at saphenous opening enlarged. The attack began with chill and fever. Blood examination: Red blood corpuscles, 3,710,000; hæmoglobin, 74 per cent.; white blood corpuscles, 4160.

December 17th. Another attack of right-sided orchitis.

January 7, 1901. Diarrhœa.

17th. Considerable hemorrhage after extraction of a tooth.

February 17th. Chill; temperature, 101°; facial erysipelas.

March 4th. Pain in right elbow.

19th. Marked pharyngitis and laryngitis. Some impairment of resonance in right chest. Mucopurulent blood-streaked sputa. No tubercle bacilli. Daily fever in afternoon. Blood: Red blood corpuscles, 4,670,000; hæmoglobin, 60 per cent.; white blood corpuscles, 1920.

May 8th. Another attack of right orchitis.

June 10th. Recently complains of pain in region of spleen.

16th. Much pain in right arm.

July 8th. Marked diarrhœa. Blood: Red blood corpuscles, 2,950,000; hæmoglobin, 45 per cent.; white blood corpuscles, 2720.

October 15th. Liver smaller, lower border only two fingers' breadth below costal margin. Hair growing very white. Pain in right arm continues.

22d. Blood: Red blood corpuscles, 4,060,000; hæmoglobin, 61 per cent.; white blood corpuscles, 2460. Differential count: Polymorphonuclear, 78 per cent.; mononuclear, 6.52 per cent.; transitional, 6.5 per cent.; lymphocytes, 6.5 per cent.; eosinophiles, 2.5 per cent.

November 11th. Thickening about right elbow-joint.

February 5, 1902. Blood and mucus from bowel. Fistula discovered.

March 4th. Increased diarrhœa. Patient's strength failing greatly. Blood: Red blood corpuscles, 3,160,000; hæmoglobin, 64 per cent.; white blood corpuscles, 10,600.

8th. Blood: Red blood corpuscles, 3,890,000; hæmoglobin, 68 per cent.; white blood corpuscles, 11,040. Unconscious and restless during night; died in stupor.

Autopsy. (Dr. Hendrickson, pathologist.)

Pathological Diagnosis. Pigmentation of skin and jaundice; chronic splenic tumor; atrophic cirrhosis of liver; acute lobar pneumonia; chronic interstitial orchitis; arteriosclerosis of aorta; chronic arthritis of right radiohumeral joint.

Detailed Description of the Organs. External Appearance. Body that of an extremely emaciated and poorly developed white male. Mucous membrane pale; rigor mortis absent; no œdema; considerable post-mortem lividity of dependent portions. Over sacrum is discovered a small bed-sore about 3 cm. in diameter and superficial in character. There is marked jaundice with a brownish pigmentation of the skin. The distribution of the pigment is confined entirely to the extremities. It is found over lower extremities below the knees in large, irregular patches, which are more or less confluent; the intervening areas of skin are of normal appearance. The same pigmentation is found over the hands and forearms. Fingers show marked clubbing. Superficial lymph nodes not enlarged.

Abdominal Cavity. Spleen is found enlarged and projects about 6 cm. below the costal margin. Upper border firmly adherent to the under surface of diaphragm. Liver does not extend below the costal margin except in the epigastric spaces, where it projects 3 or 4 cm. below the xiphoid process. Otherwise cavity negative. Mesenteric lymph nodes not enlarged.

Pleural Cavities. Negative.

Pericardial Cavity. Negative.

Heart. Weight, 270 grams; normal except myocardium, which is paler than it should be.

Lungs. Left: Surface dark red in color, but everywhere smooth. On section cut surface dark red and from the cut vessels considerable blood flows. Consistency considerably increased, and on pressure a marked amount of dark, bloody fluid and air escapes. The condition is uniform from apex to base. Bronchial lymph nodes deeply pigmented, but not enlarged. Right: Surface dark-red and smooth. No evidence of pleurisy. On section the lower lobe and small portion of the upper lobe are found consolidated. This part of lung is grayish-red in color, and on pressure a small amount of puriform fluid can be expressed. Middle lobe and upper portion of upper lobe are not so firm in consistency, but show marked congestion. Bronchial lymph nodes also pigmented, but not enlarged.

Spleen. Weight, 950 grams; considerably increased in size. Except where adherent to diaphragm, surface smooth. On section, capsule slightly thickened; trabeculæ prominent; pulp increased in amount and dark red in color. Malpighian bodies not visible. Consistency of the organ decreased.

Gastrointestinal Tract. Normal except at lower portion of rectum, where the mucous membrane shows marked swelling and congestion of the bloodvessels.

Pancreas. Normal.

Liver. Considerably decreased in size; surface roughly lobulated, giving rise to a typical hobnail surface. Over the anterior surface of the right lobe is found an irregular-shaped area of depression about 4 cm. in diameter, which, however, shows no thickening of Glisson's capsule. Also along the free border near the gall-bladder there is an area of depression. Section through these areas shows no scars in the depth. General appearance of cut surface is dark brownish-red, but liver tissue is divided into large areas of varying size by connective tissue. Consistency of liver distinctly increased. Gall-bladder normal.

Adrenals. Normal.

Kidneys. Of normal size; capsule strips readily; surface grayish-red in color. Weight of kidneys, 300 grams. No injection of stellate veins. Cut surface shows moderate congestion of bloodvessels, but otherwise no visible change.

Bladder and Ureter. Normal.

Prostate. Normal.

Testicle. Left, normal; right, slightly decreased in size. Slight increase in thickness of its surrounding coats. Throughout the gland proper is discovered a marked increase in grayish, firm connective tissue. Tubules do not pull out as readily from this gland as from the left.

Aorta. Shows a few scattered patches of sclerosis. None of the lymphatic glands show increase in size.

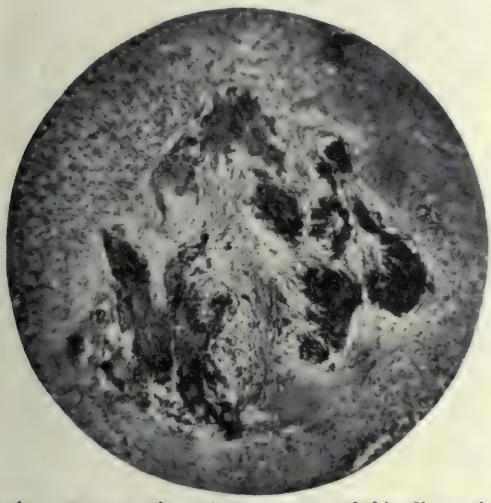
Bone-marrow. From shaft of femur is dark grayish-red in color, and of firm consistency.

Organs of Neck. Marked congestion of bloodvessels of mucous membrane over larynx and trachea. Considerable mucus in trachea. Right thyroid lobe slightly increased in size. On section, however, nothing abnormal can be discovered.

Spinal Cord. Examination without sectioning shows nothing abnormal.

Right radiohumeral joint removed *in toto.* Examination of the interior of this joint shows a superficial erosion of cartilage and bone over a small portion of the prominence separating the radial articular surface from adjacent bone. Also a more marked erosion of the articular surface in the greater sigmoid cavity of the ulna.

FIG. 8.



Coarse hæmatogenous pigment masses surrounded by fibrous tissue.

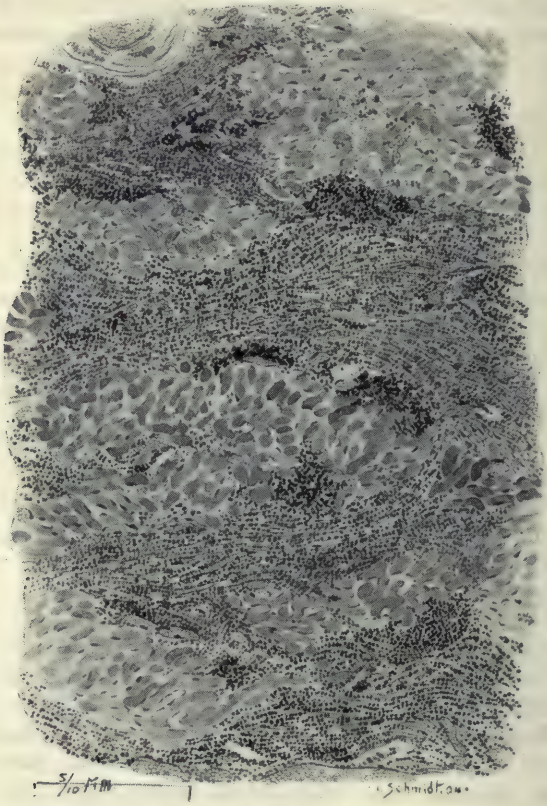
Microscopic Features. (Examination by Dr. Stengel.) *The Spleen.* There was throughout this organ a diffuse connective-tissue hyperplasia, involving the walls of bloodvessels, the trabeculæ of the organ, the splenic pulp, and the Malpighian bodies. Throughout the pulp this process was diffuse and cellular, but in and around the Malpighian bodies and elsewhere in circumscribed foci it was of a denser nature with a marked tendency to hyaline change. In a number of places a peculiar form of pigmentary deposit was observed within areas of dense fibroid tissue. In such areas brownish pigment masses of a hyaline or almost crystalline appearance were found within a focus of dense connective tissue. Stained with ferrocyanide of potash and muriatic acid these formations gave a distinct iron reaction, which, with the general appearances, showed the pigmentation to be of hemorrhagic origin. The coarse character of these lesions and the marked connective-tissue change around them gave a peculiar appearance that

I have not seen in any other spleen, excepting from one other case of similar clinical character (Fig. 3).

The connective-tissue growth in the walls of bloodvessels and surrounding them was very pronounced, and many of the smaller vessels were entirely obliterated.

In the splenic pulp many pigment cells containing rather coarse, brownish pigment were found, quite apart from the areas of marked

FIG. 4.



Section of liver. × 41.6.

pigmentation before referred to. Everywhere throughout the spleen there were foci of recent hemorrhage, sometimes side by side with older hemorrhagic pigmentation, and sometimes independent of such. Altogether there were decided evidences of congestion and hemorrhagic processes of old and recent origin with secondary fibroid and pigmentary changes. Independent of these the substance of the organ presented a diffuse fibroid change of seemingly irritative character. Under higher powers swollen and

proliferated endothelial cells were moderately conspicuous in the sinuses, but nowhere were these aggregated to form distinct masses.

The Malpighian bodies were extensively altered. Many had become converted into fibrous and hyaline masses; others were partially affected by fibrous change beginning around the central vessel; only a few were found without some alteration of structure.

The Liver. There was a very pronounced grade of connective-tissue infiltration of interlobular and intralobular character. In many places the hepatic lobules were surrounded by a dense cellular connective-tissue growth which was most markedly interlobular, but also invaded the atrophied lobules. The liver cells themselves were moderately pigmented, but were quite generally distorted and atrophied. The portal veins were widely distended, but the central vessels of the lobules were narrowly contracted and nearly free of blood (Fig. 4).

The Lymphatic Glands. All of the lymphatic glands showed diffuse, fibrous change of moderate character, and intense congestion with widely dilated blood spaces. The glands from various portions were not examined with reference to the distinctive changes in the different groups.

The Bone-marrow. The marrow from the shaft of the femur showed distinct lymphoid characters. The majority of the cells were large and small neutrophile myelocytes, with pale, eccentric nuclei. Eosinophile myelocytes were present in small numbers, and rather more eosinophile cells of the ordinary type. Some pale hæmoglobin-containing cells of doubtful nature were observed, but no distinct nucleated red corpuscles. Polymorphonuclear cells and fat cells were not numerous.

Other Organs. The sections of the lung showed decided fibroid and cellular pneumonia. There was undoubtedly an old fibroid process with more recent bronchopneumonia. The pancreas and kidney showed moderate sclerotic change. The right testicle was markedly altered, being practically converted into fibrous tissue. Several areas of hemorrhagic pigmentation, similar to the coarse pigmentation in the spleen, were found in the testicle.

CASE II. *Female, aged two years and eight months. Enterocolitis at one year; little evidence of rickets; pallor, enlarged spleen, palpable superficial lymph glands; severe anæmia, at first without, later with leukocytosis; diarrhœa, terminal tuberculosis, and endocarditis; duration one and a half years; autopsy.* Elsie S., aged two years and three months; admitted October 13, 1899.

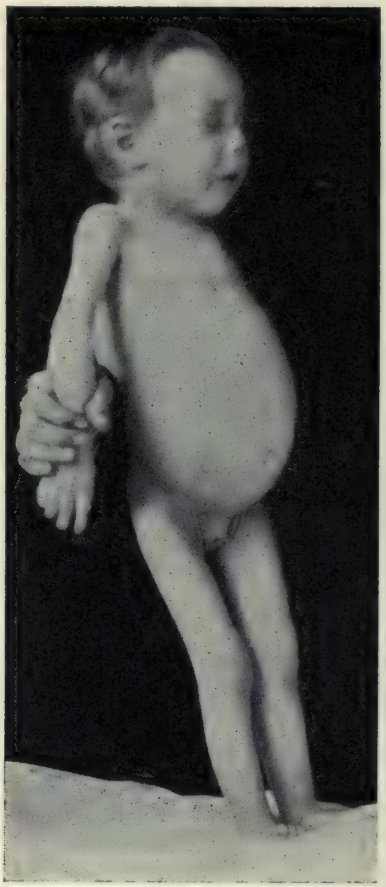
Family History. Both parents and two sisters are living and in good health.

Previous History. One year before had a severe attack of enterocolitis. The child was healthy with this exception until the present illness. Began to walk when twelve months old (Fig. 5).

Present illness began when she was twenty months old. The parents first noticed increasing size of the abdomen and pallor.

Status Præsens. Ashy pallor; slight osseous signs of rickets; abdomen large and globose, quite tense. Enlarged spleen, with notches easily palpable. Liver enlarged to percussion, but edge cannot be felt. No fluid in abdomen.

FIG. 5.



All superficial lymph glands enlarged and easily palpable. Heart is found under sternum, extending an equal distance to right and left. A short systolic, puffing murmur is heard at the left side of cardiac dulness. Breath sounds harsh, but resonance good.

Blood Examination. Red blood corpuscles, 2,920,000; hæmoglobin, 30 per cent.; white blood corpuscles, 7600. Differential count: Polymorphonuclear, 50 per cent.; mononuclear, 17 per cent.;

lymphocytes, 31 per cent.; eosinophiles, 1.6 per cent.; myelocytes, 0.4 per cent.

There was constant diarrhœa, the movements numbering from three to five daily.

October 25, 1899. The condition continues without much change. The skin has become somewhat yellowish. At this date the spleen extends a finger's breadth below the anterior superior spine of the ilium, and the anterior edge is within one-half inch of the middle line. The liver is still enlarged to percussion, but the edge cannot be felt.

The heart is now in a more normal position, extending from the third rib above to the sixth below and from left nipple line to right border of sternum. The same soft, systolic murmur is heard, but it is not transmitted beyond the cardiac borders. The point of maximum intensity is at the pulmonary region. The second pulmonary sound is not accented.

The left kidney can be plainly felt in the back, being seemingly pushed backward; the right is less plainly felt.

26*th.* Several small masses can be felt in the abdomen. They seem to disappear after a movement of scybalous masses.

November 4*th.* The submaxillary, submental, and cervical glands are distinctly enlarged.

15*th.* Moderate fever and continued diarrhœa.

December 8*th.* General urticaria followed by swelling of eyelids, face, legs, and arms.

10*th.* The swelling has disappeared.

11*th.* Blood: Red blood corpuscles, 3,920,000; hæmoglobin, 40 per cent.; white blood corpuscles, 14,720. Differential count: Polymorphonuclear, 49.2 per cent.; mononuclear, 2.4 per cent.; transitional, 12.8 per cent.; lymphocytes, 34 per cent.; eosinophiles, 1.6 per cent. Polychromatophilia; a considerable number of normoblasts.

16*th.* Physical signs the same, but liver seemingly larger. Edge can be felt. Kidneys still easily palpable in flanks.

January 27, 1900. Has been better of late. Now a greenish-yellow pallor is noted.

February 15*th.* Sudden fever, with scarlet flush of face and neck; later, papules which were bright red at first, but soon faded.

The later notes have been unfortunately mislaid, but the final phase was one apparently of disseminated pneumonia with continued fever of about 103° to 104°; respirations varying from 50 to 68, and corresponding pulse rate.

(The autopsy was made by Dr. Flexner.)

Pathological Diagnosis. General lymphatic enlargement, with congestion and hemorrhage of the glands; splenic tumor, with infarctions; anæmia of the organs; subacute, vegetative, mitral endocarditis; necrosis of the mucous membrane of the œsophagus; tuber-

culosis of the lymphatic glands and tuberculosis of the lungs; infarction of kidneys.

Bacteriological Diagnosis. Staphylococcus aureus from heart's blood; aortic valves; œsophagus; lungs.

External Appearance. Body of an emaciated, very pale child. Length 82½ cm. The abdomen is much distended. No evidence of fluid. The spleen can easily be felt in the left hypochondriac region. Its lowest border is 21 cm. in the midaxillary line below the ribs. The circumference of the abdomen below the ribs is 47½ cm., and just above the umbilicus 43½ cm. There is a very small amount of subcutaneous fat; indeed, it is in most places absent. There is very slight œdema of the lower borders of the ribs. Over the extremities, particularly the lower extremities, are minute, petechial hemorrhages. Over the abdomen are several pigmented depressions, which are probably the remains of small furuncles. No rigor mortis.

Abdominal Cavity and Peritoneum. Upon opening the abdominal cavity the omentum is seen to be adherent to the greatly enlarged spleen. Upon being stripped back, which can be done in part only on account of the old adhesions, it is found that there is a fresh exudate of yellow fibrin over the upper part of the enlarged organ. In the lower border there is an infarction about 2 cm. in width. The surface of the spleen is mottled, the predominating color being brown, and lighter areas corresponding to other infarctions can be seen on its superficial surface. There are no adhesions, excepting to the diaphragm on the upper edge, with the exception of those to the omentum as already described. The spleen weighs 465 grams. Its measurements are 17 x 9 x 5 cm. Its consistence is firm and even very hard. On section the infarctions described are found to be on the anterior surface; they are three or four in number, varying from 1½ to 3 cm. in their widest portion. They are either anæmic or mixed in character. The mixed ones show a cortical anæmic layer and a deep brownish-red, rather soft, central portion. They extend about 2 cm. into the substance of the organ. In other portions the spleen is of a reddish-brown color, and there is no distinction of Malpighian corpuscles. Here and there on the cut surface are whitish points about the size of pinheads, which are taken to be small, dense thrombi.

Liver. With the exception of an adhesion on the anterior surface of the right lobe to the abdominal wall, measuring 1½ cm. in diameter, and very old in nature, it is free from adhesions. Its weight is 690 grams. Its cut section is cloudy. Its consistence is not increased.

Kidneys are alike. The capsule strips off easily, showing in each organ a recent infarction about 4 mm. in diameter in the cortex, about which the tissues are greatly congested or hemorrhagic. On section the cortex is pale, pyramids somewhat more injected. Be-

neath the mucous membrane of the pelvis there is a reddish accumulation which looks like tissue, or may be hemorrhage. Adrenal glands appear normal.

Heart and Pericardium. Pericardial cavity contains about 30 c.c. of clear, yellow fluid. The layers of the serosa are smooth. The right ventricle is dilated. The left ventricle is contracted. The heart's flesh is pale. The tricuspid, pulmonary, and aortic valve segments are delicate. The mitral segments are covered with vegetations, quite adherent, which average in size about a bird-shot, some being larger, and as large as a hemp-seed. The two edges of the valve are rather difficult to separate, but this union is due probably to a small clot formed post-mortem over the edge. In the diaphragm there are scattered whitish points, probably tubercles.

Lungs. The right lung is bound over the upper portion of the upper lobe to the chest wall. The left lung is bound over the apex to the chest wall. There is no fluid in the pleural cavities. The lungs are insufflated. On section the upper lobes contain disseminated, gray tubercles; fewer in the lower lobes. There are no definite foci of consolidation, although in the pleura over each upper lobe are small hemorrhages. Beneath the parietal pleura on the left side, and following the intercostal muscles, are found white or caseous areas of tuberculosis. In the bifurcation of the trachea there is a large gland, the size of a pigeon's egg, which upon section is completely caseous.

Stomach and Intestines. The stomach shows nothing of special interest. Post-mortem digestion. The duodenum contains a number of elevated, swollen, solitary follicles, after which there is no swelling of any of the follicles throughout the length of this intestine. In the lower part Peyer's patches are visible, but nothing more. The mucous membrane of the large intestine is attenuated. In general, the intestine is thin and apparently atrophic.

Tonsils. Enlarged, and there are irregular depressions. No definite foci can be made out. In the upper part of the œsophagus, on a line with the upper part of the thyroid cartilage, there are two foci of necrosis, each about 4 mm. in width, over which there is a dirty-white exudate.

Lymphatic Glands. The inguinal, axillary, and cervical glands can easily be made out by palpation. The glands of the neck cause the tissue on each side to project. All the lymphatic glands of the body, upon examination, are found to be enlarged and to be very red in color. The greatest enlargement is found in the cervical and in the inguinal regions, in both of which places the superficial as well as the deep sets are swollen. The swelling affects the individual glands and not the invading tissue. In the cervical region the largest gland is about the size of a pigeon's egg. Most of them vary from a pea to a cherry in size. In the inguinal region the largest

is about the size of an almond. The retroperitoneal glands form chains and large, red bodies. The mesenteric glands and the glands in the mesocolon and the omentum are all enlarged and congested or hemorrhagic. The glands about the pancreas are especially enlarged. Some of them contain whitish nodules, evidently tubercles. The largest of the mesenteric glands contain also a white area, suggesting tuberculous caseation.

Bone-marrow. The bone-marrow of the femur is abundant and red in color. Its consistence is soft.

Microscopic Features. (Dr. Stengel.) The sections of the spleen varied considerably in their appearances according to the part of the organ from which they were taken. Those from the areas of infarction showed only the usual features of dense hemorrhagic infiltration and pigmentation. In other parts the splenic tissue was markedly sclerotic, and sections stained with Biondi's or Van Gieson's stain presented a uniform, rather dense, fibrous reticulum. Hyperplasia of the endothelial cells of the sinus was evident in some places, and large (swollen) endothelial cells of rounded or irregular shape, with one or a few pale nuclei, were found scattered through the spaces. In a few areas groups of such cells were seen lying together. The proper splenic pulp and the Malpighian bodies had undergone an evident atrophy, and many of the latter were converted into hyaline material. A few doubtful miliary tubercles were seen in the sections. These consisted of a small giant cell surrounded by a group of round (lymphoid) cells. There was no evidence of necrosis.

Lymphatic Glands. The sections of mesenteric lymph glands showed marked thickening of the capsules and of the trabeculæ, the latter separating the lymph follicles in an unusually marked manner. The medullary part of the glands was occupied by numerous widely distended blood spaces or vessels. The lymphoid tissues proper showed no special alteration, but decided proliferation of endothelial cells of the sinuses was seen in places, and numerous macrophages containing one, two, three, or more erythrocytes or fragments of such were found. The red corpuscles within the lymph sinuses were much broken, and everywhere fragments of irregular or more commonly rounded shape, and with distinct basic staining reaction, were found among the degenerated erythrocytes. These fragments were of precisely the appearance of blood plaques, and from their situation and general character could be plainly recognized as derivatives of degenerated red corpuscles.

The Liver. Marked lymphoidal and leukocytic infiltration between the columns of liver cells was the most striking feature of the sections as seen under a low form. In areas there was distinct interlobular fibrosis surrounding the portal vessels. The latter were considerably dilated and, besides containing fragmented and degenerated red corpuscles as well as normal erythrocytes and leukocytes, in many places also contained numerous plaque-like forma-

tions such as have been described for the lymphatic glands. Here and there in the dilated portal vessels could be found large endothelial cells of the same appearance as those of the spleen and lymphatic glands. These were distinguishable from the lining endothelium of the bloodvessels of the liver, and if derived from this source had manifestly undergone secondary change. No such cells could be found outside of the bloodvessels. They were too numerous and widespread to be attributed to accident or artefact.

The Lung. The lung tissue in general showed no marked alterations in the sections examined, but a few peribronchial miliary tubercles were seen in portions especially selected to determine the nature of the gray bodies observed at the autopsy.

The Bone-marrow. Unfortunately the material was lost and microscopic examination could not be made.

CASE III. *Female, aged twenty-one years, married, two stillborn children; probable onset years before; enlarged spleen, palpable superficial lymph glands, pain in left side, slight anæmia, splenectomy; postoperative pneumonia; recovery; histological examination of spleen.*—Annie D., aged twenty-one years, negro; lived in North Carolina until a year ago, when she came to Philadelphia. Had two stillborn children about a year ago. Her father died of malaria, her mother of an accident. No brothers or sisters. The patient has always been in good health; menses always regular and normal. She says that for many years there has been more or less pain in the left side of the abdomen. She cannot tell exactly how long this has been. Until three months ago the pain was not, however, severe enough to keep her from attending to her usual duties, but during the last three months it has been so severe at times as to compel her to take to bed. During the same length of time she has noticed a lump in the left upper abdominal quadrant. The pain is dull and aching in character, but becomes more severe when the patient moves about. There has been some loss of weight during the last three months.

Status Præsens. The patient is fairly well nourished, looking somewhat older than her years. There is nothing striking on external examination excepting a projection in the left upper half of the abdomen. The superficial lymphatic glands, cervical, axillary, inguinal, and epitrochlear, are all palpable. Heart and lungs normal. Occasionally a short systolic murmur was heard over the root of the pulmonary artery.

Abdomen. There is marked prominence of the left side above. This moves downward on full inspiration. On palpation a greatly enlarged spleen could be palpated and was distinguishable by the notches in front. At first palpation was somewhat difficult on account of tenderness, but later the patient seemed to be suffering less pain. The mass extended downward and forward to within an inch and a half of the linea alba at the level of the umbilicus, and

to about the level of the crest of the ilium below. The posterior border is felt as a thick, rounded surface, while the anterior border has a fairly sharp edge with a distinct notch. No nodules or irregularities can be felt along the edge above the ribs. The mass extended to the sixth rib. The liver extended from the sixth rib to the edge of the ribs. It was not palpable. The stomach was crowded upward and forward, as could be determined by inflation, and the colon was pushed downward.

Blood. Red blood corpuscles, 4,440,000; white blood corpuscles, 5600; hæmoglobin, 70 per cent. The stained specimens show a slight reduction in the color of the red blood corpuscles, but no other peculiarities were discovered. Degenerative changes, such as polychromatophilia and basic degeneration, were wanting. The differential count of the leukocytes at this time showed no marked peculiarities, though the count has been lost.

Urine. Specific gravity, 1020; amber color, acid, no albumin, no sugar. Microscopically granular precipitate, epithelial cells, and a few leukocytes were found.

The patient was kept under observation for some weeks, during which the condition remained practically unchanged. There was apparently no increase in the size of the spleen and no change in the patient's general condition excepting perhaps a decrease in the amount of pain. Her weight remained exactly the same. It was decided that the case was one of splenomegaly and that, on account of the pain and incapacity of the patient, operation was desirable. For this purpose she was returned to the service of Dr. John G. Clark, who originally had referred her to me, and who has kindly permitted me to report the case.

On the day preceding the operation the differential count showed the following figures: Lymphocytes, 29 per cent.; mononuclear, 7.4 per cent.; transitional, 5.4 per cent.; polymorphonuclear, 50 per cent.; eosinophiles, 7.8 per cent.; basophiles, 0.4 per cent. The subsequent leukocytic counts following the operation will be seen in the table on the opposite page.

The operation of splenectomy was performed by Dr. Clark on January 28, 1904. The following notes were recorded at the time: The spleen was rather dense in consistency and the surface showed numerous nodules about 1 to 2 cm. in diameter, with depressed centres. The relations of the organ were found as described in the physical examination. There were a few adhesions posteriorly and some in front, between the lower border of the tumor and the great omentum. These were tied off; the others gave no trouble. The splenic vessels were ligated with some difficulty on account of the very narrow space between the tail of the pancreas, the cardiac end of the stomach, and the spleen. The liver was slightly enlarged and showed a number of scar-like depressions on the surface of both lobes.

Date.	Red blood corpuscles.	Hæmoglobin.	Leukocytes. Total count.	Lymphocytes.		Mononuclear.		Transitional.		Polymorphonuclear.		Eosinophile.		Basophile.	
				%	No.	%	No.	%	No.	%	No.	%	No.	%	No.
Jan. 1, 1904	.....	.....	5,600												
" 27, "	.....	.....	.....	29.0	.....	7.4	.....	5.4	.....	50.0	.....	7.8	.....	0.4	
" 29, "	.....	.....	.....	5.0	.....	4.2	.....	4.0	.....	86.5	.....	0.2			
" 30, "	3,750,000	55 %	35,000	3.0	1050	4.4	1540	7.6	2660	84.8	29,680	.....	.....	0.2	70
" 31, "	.....	62 %	16.640	5.0	832	2.5	416	10.2	1697	74.4	12,380	3.6	599	0.5	83
Feb. 1, "	3,350,000	.....	12,720	3.4	432	2.4	305	8.2	1043	74.8	9,514	10.5	1335	0.3	38
" 2, "	.....	.....	21,120												
" 3, "	.....	.....	21,760												
" 4, "	4,190,000	55 %	17,680												
" 6, "	.....	.....	21,120												
" 10, "	.....	.....	20,000	6.6	1320	2.2	440	7.8	1560	81.0	16,200	2.4	480		
" 14, "	3,840,000	.....	21,520												
" 16, "	.....	.....	23,860												
" 18, "	.....	.....	9,600	9.0	864	2.6	250	9.6	921	70.7	6,787	7.9	758	0.2	19
" 24, "	.....	.....	9,000												
Mar. 14, "	4,030,000	55 %	9,120												
May 5, "	4,900,000	55 %	7,280	18.6	1354	2.8	204	5.7	415	61.9	4,506	11.0	800		

Almost immediately after the operation the patient complained of pain at the base of the left chest and in the left upper part of the abdomen. The temperature rose to 102° and subsequently kept constantly above normal. At first physical examination was difficult because of the impossibility of turning the patient, but indefinite rales or friction sounds were heard. Later decided signs of a lobar pneumonia were detected. Before this time, however, the upper angle of the incision was opened in the effort to discover the cause of the pyrexia, and a small area of induration, but no suppuration, was discovered. On February 17th, twenty days after the operation, and after the first elevation of temperature, the fever subsided by crisis, going from 103° to the normal in the course of a few hours, and remaining normal continuously thereafter. At the same time the leukocytes declined from over 20,000 to 9600, and subsequently remained normal or subnormal.

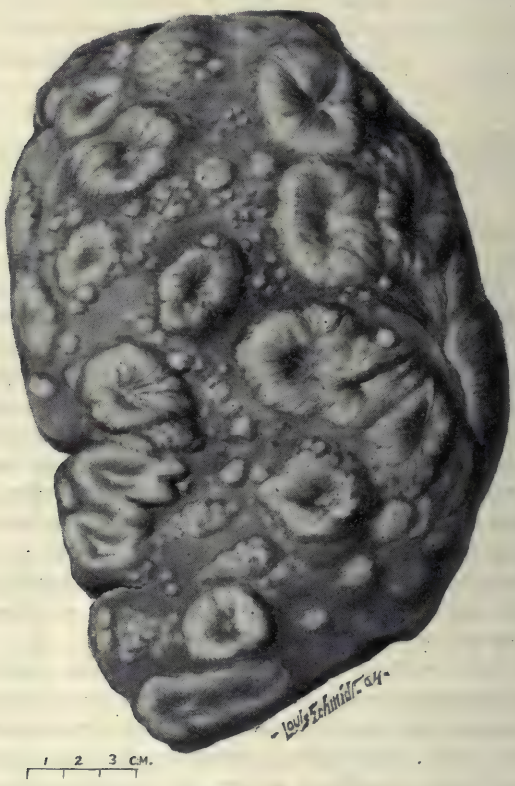
After the full recovery from the operation the patient showed no change in appearance or physical signs, excepting those referred to the left upper part of the abdomen. She complained of some dragging and other unpleasant sensations in this region, but as compared with her condition before the operation was certainly much relieved.

Three months after the operation I found her in comparatively good health, able to attend to her work as a chambermaid, and with practically no local symptoms. The lymphatic glands seemed to have increased somewhat in size, but the difference was not very marked.

Among the interesting features in the blood count of the case was the behavior of the lymphocytes and eosinophile cells. It has been found by experiment, as well as after operative removal of the

spleen in man, that there is an increase in the number of lymphocytes and later an increase in the eosinophile cells. The proportion of the latter was at the time of the operation decidedly increased (7.8 per cent.). The lymphocytes were not specially increased (29 per cent.), but the polymorphonuclear cells were actually and relatively reduced in number. This reduction was, however, in favor of the mononuclear and transitional cells, which at this time and subsequently showed conspicuous increase.

Fig. 6.



Spleen. × ½.

Unfortunately the intervention of an acute pneumonia altered the figures that probably would have been obtained. The result of the postoperative pneumonia are the same as is usually seen in normal persons—a marked polymorphonuclear leukocytosis and a reduction of eosinophiles. After the subsidence of the pneumonia there was a return to practically the same conditions as were observed before operation, viz., a marked eosinophilia and reduc-

tion of polymorphonuclear in favor of the mononuclear and transitional cells.

Macroscopic Appearance of the Spleen. The organ measured 22 x 13 x 7 cm., and after hardening weighed 1230 grams. The striking features when seen in the fresh state were numerous nodular projections on the surface, which presented the appearance of secondary tumors. These varied in size from small masses a half to 1 cm. in diameter up to large nodes fully 2½ or 3 cm. in diameter. The larger nodes were distinctly umbilicated, the depression being quite marked and of a whitish, cicatricial appearance at the bottom. Elsewhere the surface of the organ was red in color, somewhat modified by a more or less thickened capsule. The project-

FIG. 7.

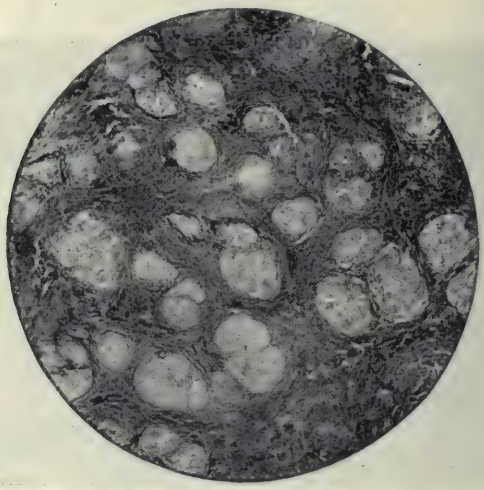
Macroscopic appearance of section (photograph). The lighter areas represent new-growth; the darker areas are uninvolved splenic tissue.

ing nodules were numerous anteriorly and on the convex surface of the organ; they were fewer posteriorly and in the hilum. The consistence of the organ as a whole was distinctly increased and was uniform in all portions. On section through its substance practically the entire organ was seen to have been invaded by a growth of a dense consistence and pinkish-red color. This extended inward and toward the hilum, leaving only small parts of the substance of the spleen, which could readily be distinguished by their darker color, uninvolved. Posteriorly and at the hilum the spleen substance was comparatively free. As seen in the cross-section the nodular masses on the surface were manifestly not separate new-growths like secondary tumors, but projecting parts of a large invading mass which occupied the greater part of the organ. The

appearance was not unlike such a one as might result from separate pyramidal growths, with the apices projecting from the surface of the organ and extending deeply into the substance, the bases being completely fused or at most leaving small areas of normal splenic tissue here and there between them (Figs. 6 and 7).

Careful examination of the umbilications of the nodules presented no evidence that these had resulted from secondary softening of the centres of the growths, but suggested rather that the elevation surrounding the depressions was the result of an infiltrating process that had not affected the centre so that the fibrous tissue of trabeculæ had prevented the elevation at the point of umbilication. Cross-sections showed some excess of fibrous tissue in this central

FIG. 8.



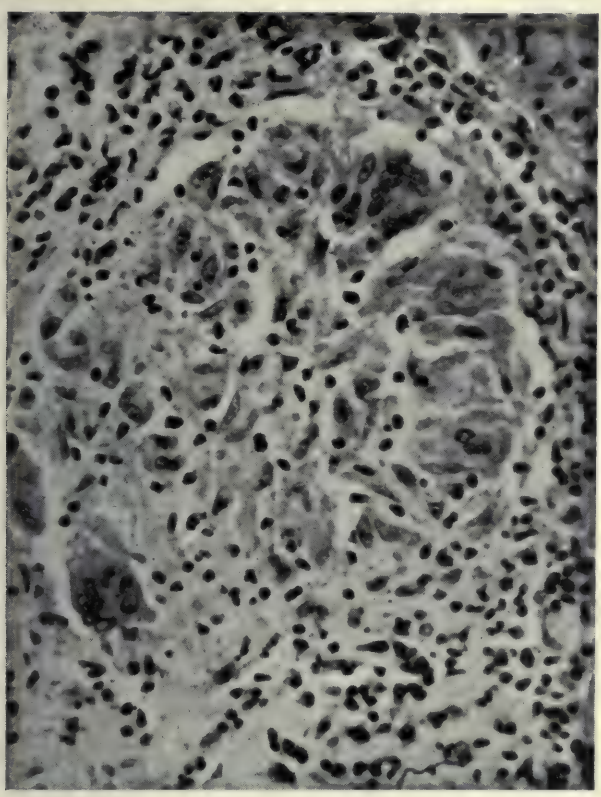
Microphotograph of section of spleen under low magnification, showing the alveoli containing endothelial cells surrounded by fibrous walls. The photograph exaggerates the density of the fibrous tissue.

zone, and the cicatricial appearance on the surface was due to thickening of the capsule of the spleen at the point noted, quite as much as to actual fibrous tissue formation in the centre of the nodes. Nowhere in the substance of the new-growth could any evidence of necrosis be discovered by the naked eye, no areas of softening, of caseation, or the like. The tissue was uniform in character, somewhat glistening on section and, as before stated, pinkish-red in color.

Microscopic Appearances. Portions of various parts of the organ were placed in Zenker's fluid, Müller-formol, and absolute alcohol, and sections were stained with eosin-hæmatoxylin, Van Gieson's stain, Biondi's mixture, carbol-fuchsin, methylene blue, and by Gram's method.

The sections showed a marked new growth of connective tissue forming alveoli of various sizes (from 0.13 to 0.26 mm. in diameter), and containing large, clear cells, with pale nuclei, and often cells containing several nuclei of the same character. In certain areas giant cells with centrally or eccentrically clustered nuclei were abundant, and everywhere such cells were present, at least in small numbers. The lymphoid elements of the splenic pulp were an

FIG. 9.



Microphotograph (high power), showing one of the alveoli containing endothelial cells, giant cells, and leukocytes.

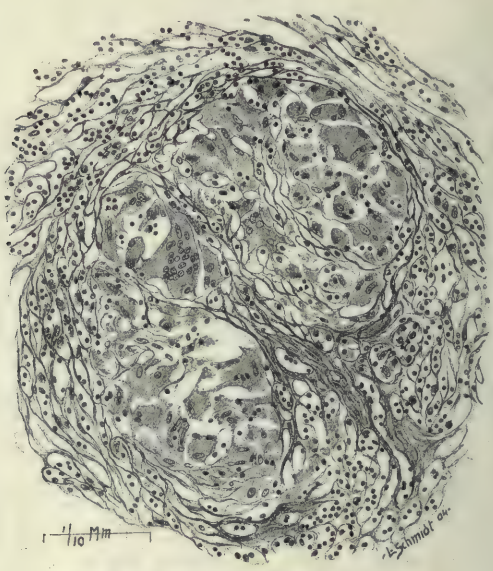
inconspicuous feature in all the sections, being crowded into mere zones surrounding the alveolar formations where these were well developed, and being displaced by more diffuse connective-tissue growth in other places.

The alveolar spaces referred to were generally rounded in outline and surrounded by a wall of well-developed connective tissue of considerable thickness. For the most part this wall was compact

and separated from the surrounding alveolar or splenic tissue by a sharp line of separation, but elsewhere the transition was more gradual and formed by connective tissue of a less dense character intermixed with lymphoid elements (Figs. 8, 9, 10 and 11).

Within the alveoli were found the large endothelial cells before described. In sections through favorable parts of the growth the cells were separate and clearly marked, but more commonly there was an apparent or real confluence making large protoplasmic structures containing large vesicular nuclei. These almost invariably showed nucleoli. Many of the cells contained two or three nuclei. In the peripheral parts of the alveoli, and to a less extent in the

FIG. 10.



Section of spleen. Biondi's stain. × 142.5.

centre, giant cells with clusters of nuclei were common. The protoplasm of the cells was clear and rather glistening. It did not present any appearance of degeneration, though in some places it was possibly somewhat hyaline. In some of the alveoli, especially those with less well-developed walls, the endothelial cells were separated by or intermixed with erythrocytes or lymphoid cells, but there were no macrophages. Pigmentation was practically absent in this part of the tissue, but was present to a small extent in the reticular connective tissue.

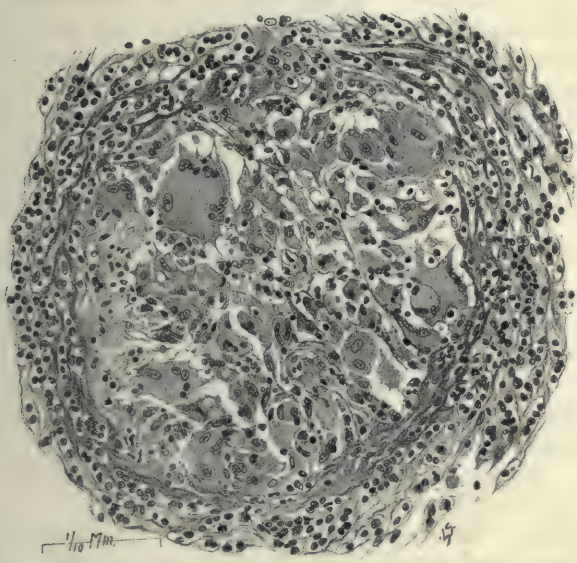
The size of the endothelial cells containing one or two nuclei varied from about 10μ to 20μ in diameter, the average being about 15μ; the size of the giant cells was from 30μ to 72μ, the average of

a number being 51μ. The large masses of fused character were even larger, in some places nearly filling the alveolus.

In the portions of the spleen comparatively free from the uniformly infiltrating growth there was still evidence of an active endothelial proliferation, but as the organ was practically entirely involved it cannot be determined if this process were simply an extension from the growth proper or an evidence of prior involvement in lesser intensity of a condition that caused complete transformation in the parts that have been designated the growth proper.

The Malpighian bodies were retained in some places, though atrophied. Elsewhere they were converted into connective tissue

FIG. 11.



Section of spleen. Mallory's stain. × 157.

or had become hyaline. This, however, was an inconspicuous feature. In general the endothelial and fibrotic process had simply caused a disappearance of normal splenic features.

In sections from one part of the spleen the Malpighian bodies were conspicuously involved, being occupied by a rounded, acinus-like area of endothelial proliferations, lying adjacent to the blood-vessel of the Malpighian body and sometimes pushing the vessel to one side, but never involving it. In some parts the area of endothelial character was minute; elsewhere almost the whole Malpighian body was transformed. There was no evidence of fibrous-tissue formation in these areas.

Sections stained with carbol-fuchsin and Gabbett's solution

showed *no tubercle bacilli*, and those stained by Gram's method likewise showed no bacteria of any kind.

CASE IV. *Man, aged fifty-one-years; history of malaria, stunted growth, pigmented skin, clubbed fingers and toes, enlarged abdomen (tympany), enlarged spleen, slightly enlarged liver, moderate anæmia, leukopenia, diarrhœa, hemorrhages from bowel, rectal ulceration, tendency to chills, no malarial organisms; duration at least three years, probably longer.*—C. T., aged fifty-one years, laborer on railroad, a native of Italy, had come to America six years before. Admitted to Pennsylvania Hospital September 30, 1901.

Family history negative. He himself had had some operation for a mass in the right inguinal region forty years before. During ten years after he was twenty years old he had mild attacks of chills and fever every summer. At thirty-three had some kind of bloody diarrhœa for six weeks. Six weeks ago first had pain in the left side of abdomen and distention of the abdomen and diarrhœa. The stools were free of blood, but the patient had much rectal pain.

On physical examination the patient was found a small-sized man with darker skin than the average Italian and distinct pigmentation in places. The fingers and toes showed clubbed extremities. The abdomen was enlarged and tense, but did not contain free fluid. The spleen could be felt extending far down into the abdomen. The liver dulness was small in vertical extent. Later the abdominal distention subsided and the spleen was then found extending to within an inch of the anterior superior spine of the ilium. Rectal examination showed an ulceration in the anterior wall of the rectum (Fig. 12).

Blood Examination. Red blood corpuscles, 4,190,000; hæmoglobin, 60 per cent.; white blood corpuscles, 4000.

Urine. Specific gravity, 1012; acid; some albumin present; granular and epithelial casts.

The sputum contains no tubercle bacilli. The feces contain no amœbæ; the blood serum does not agglutinate Shiga's bacilli.

March 5, 1902. Chill, temperature of $104\frac{1}{5}°$; tongue greatly swollen. Later, ulceration under tongue. Leukocytes 11,400. No malarial organisms.

April 1*st.* Admitted to University Hospital. Same conditions noted; also enlargement of practically all superficial lymph glands. Liver extends from sixth rib to two inches below ribs. Edge easily felt. Spleen as before. A small ventral hernia.

4*th.* Blood: Red blood corpuscles, 3,980,000; hæmoglobin, 70 per cent.; white blood corpuscles, 4400.

10*th.* Hemorrhage from bowel; diarrhœa.

June 6*th.* Hemorrhage from bowel, about eight ounces; diarrhœa.

7*th.* Considerable hemorrhage from bowel; chills, but no fever.

August 12*th.* Slight hemorrhage, followed by temperature of $102\frac{2}{5}°$, soon normal.

From this date no notable changes. The patient frequently complained of abdominal pain near the umbilicus (ventral hernia), in the left side (spleen), and in the rectum (ulcers). Repeated examinations showed persistence of the ulcers. At intervals he had accessions of cough, with rough breathing and rales. The blood was examined repeatedly and was found in about

FIG. 12.

the same condition as above recorded. Constant diarrhœa and frequent hemorrhages were the marked symptoms. The patient was transferred to the Philadelphia Hospital.

This case in its general appearance and in the tendency to repeated infections resembled Case I. very closely. Studies of the blood serum were made to determine if any explanation of the tendency to infection might be found. Dr. J. S. Evans, who conducted

these examinations, reported an increase rather than reduction in both immune bodies and complements. The mechanism of the infections must therefore be sought in some other direction.

CASE V. *Woman, aged forty-four years; doubtful history of malaria, enlargement of spleen, succeeded by evidences of hepatic cirrhosis (ascites); no anæmia, hydrothorax; duration two and a half years or more.*—Ellen D., aged forty-four years, white, married. Was admitted to the University Hospital November 24, 1903. The following history was recorded:

The patient is a widow and has five children, all of whom are well. She has worked hard all her life.

The family history is negative excepting that one brother died of consumption. No history of new-growths.

Menses began at thirteen years, always normal. Labors normal. The last one eighteen years ago. There was some uterine trouble six years ago and she was confined to bed for six weeks. She had malaria two years ago, but her description of the symptoms is not very convincing.

About two years ago the patient first noticed some enlargement on the left side of the abdomen. This continued without any local symptoms excepting a slight feeling of fulness and occasionally moderate pain. There has been no loss of weight, but she has become weaker. Her color has at times been a trifle sallow. A little swelling of the feet has recently developed. This comes on during the day and disappears at night. Physical examination showed slight pallor and a subicteric hue of the skin, but no distinct jaundice. Very slight œdema of the legs and feet. No cyanosis. Lungs normal, excepting that the breath sounds appear a little harsh. Heart normal in size; the first sound at the apex is a little lacking in muscular quality, but there are no murmurs. The abdomen is enlarged, especially on the left. The spleen can be easily felt, and on the anterior surface are several distinct notches. The lower border extends below the umbilicus.

The liver extends from the sixth rib to below the costal margin. As the abdomen is generally distended it cannot be plainly felt beneath the ribs, but in the epigastric spaces the edge is distinctly palpable and the substance of the organ is evidently hard and rough. There is decided movable dulness and fluctuation in the peritoneum.

Examination of Blood. Red blood corpuscles, 5,500,000; white blood corpuscles, 8800; hæmoglobin, 81 per cent.

Urine. Clear, brownish-red; specific gravity, 1025; no albumin, no sugar; urates, a few leukocytes, and epithelial cells.

November 28, 1903. Paracentesis of the peritoneum was performed and eleven pints and three ounces of clear fluid, yellowish-green in color, were removed. The liver could then be plainly felt and was decidedly hard.

30th. Some pain at the right base and a pleural friction sound. Blood: Red blood corpuscles, 5,300,000; white blood corpuscles, 7200; hæmoglobin, 80 per cent.

December 1st. Considerable reaccumulation of abdominal effusion. Right-sided hydrothorax.

5th. Increase in effusion in right chest; white blood corpuscles, 7400. Urine: Specifie gravity, 1030; small amount of albumin, leukocytes, a few red blood corpuscles, urates, a few hyaline casts. There is a trace of bile.

16th. Abdomen tapped; twelve pints fourteen ounces removed.

January 3, 1904. Abdomen tapped; sixteen pints fifteen ounces removed. The fluid does not contain bile.

14th. Abdomen tapped; eighteen pints eight ounces removed. Right pleural cavity tapped; fourteen ounces of blood-tinged fluid removed. Soon after this the patient passed out of observation.

The most interesting feature in this case was the fact that she had been under my observation a year previous to her admission to the hospital, at which time I found great enlargement of the spleen without a single symptom of consequence. It was not until long after that time that she first showed evidences of beginning cirrhosis and portal obstruction. There was not in the history of this case any hemorrhage nor the usual gastrointestinal symptoms met with in splenic anæmia.

Classification of Splenic Anæmia. Analysis of the clinical descriptions and pathological features of many of the cases classified as splenic anæmia discloses the fact that these cases properly belonged to one or the other of the following conditions:

1. *Progressive Pernicious Anæmia or Intense Secondary Anæmia.* The oft-cited case of Strümpell belongs to this group. In that case, probably one of pernicious anæmia, simple congestion with great dilatation of the splenic sinuses constituted the pathological condition of the spleen. Other cases in which pronounced anæmia and moderate enlargement of the spleen have been found should be included in this group, and these constitute the basis for the view now seldom expressed, that splenic anæmia and progressive pernicious anæmia are closely allied. As a matter of fact, in the conditions nowadays classified as splenic anæmia impoverishment of the blood is rarely a predominating feature except after repeated hemorrhages.

2. *Pseudoleukæmia.* The earliest writers (Griesinger, H. C. Wood) suggested that the condition is usually a splenic variety of Hodgkin's disease, and this view is occasionally expressed at the present day. This opinion was adopted by Sippy in his admirable review of the subject, but is now generally abandoned for the reason that the pathological anatomy as far as known almost invariably

negatives the supposed pseudoleukæmic nature of the disease. Nevertheless there are some cases reported in older (Müller) and more recent literature in which the symptoms and such pathological data as were obtained show that splenic pseudoleukæmia may be, clinically, nearly if not quite identical with that we now call splenic anæmia. Such cases are, however, exceptional.

3. *Leukæmia.* All systematic writers call attention to the occasional subsidence of leukocytosis in this disease. Under these circumstances the case might for a time have many of the clinical features of splenic anæmia, and some authorities (Griesinger) regarded the latter as an aleukæmic variety of splenic leukæmia.

4. *Cirrhosis of the Liver.* Some degree of splenic enlargement is habitual in cirrhosis of the liver. Formerly this was attributed to congestion of the spleen caused by obstruction of the portal circulation, but more recently the view has gained ground that the splenic condition results from the action of the same irritant as that which causes the cirrhosis (alcohol, etc.). Under these circumstances it might seem natural that certain cases of cirrhosis should present an unusual degree of splenic enlargement. The studies of Banti, showing a frequent association of splenic anæmia and cirrhosis, gave additional color to this view, and seemed to justify the expression *splenomegalic cirrhosis of the liver.* On the other hand, however, the investigations of Banti, Bovaird, and others showed that clinically as well as pathologically the cirrhotic process may be demonstrably secondary to the splenic disease. Under such circumstances the condition is rather one of *splenomegaly with cirrhosis.* The cases in which pronounced splenomegaly is simply an incident in cirrhosis are probably rare as far as accurate studies would indicate.

5. *Hypertrophic Cirrhosis of the Liver* (Hanot's disease). In this condition the long duration of the disease and the considerable degree of splenic enlargement are the basis upon which inclusion under the head of splenic anæmia has sometimes been suggested if not justified. Some of the cases of familiar splenic anæmia in particular may perhaps be more properly classified here.

6. *Chronic Splenitis.* The greatest confusion exists in the case of splenic enlargement in children. Such enlargement is common in rickets and congenital syphilis, and occurs in the uncertainly classified condition called anæmia infantum pseudoleukæmica (von Jaksch). In the case of rickets and congenital syphilis the splenic lesion is a chronic splenitis leading to fibroid change and some lymphadenoid hypertrophy. Clinically the dominating symptoms are those of the underlying affection. It is, of course, possible that exceptionally the splenic enlargement and its consequences might overshadow other features, but the evidence at hand does not bear out such an assumption. In the case of von Jaksch's disease, path-

ological studies and accurate clinical observations also are still wanting.

The chronic splenitis of malaria belongs in the same group. How far malaria may prove to be a factor in the etiology of splenic anæmia remains unsettled. Undoubtedly, however, there is some added element that operates in the development of the condition even if malaria is a factor.

Leaving out of consideration the cases of splenic enlargement, which by their clinical features or pathological lesions could be plainly referred to the above groups, there remain certain cases in which the splenic disease is of such dominating character that the cases must be regarded as forming a separate group or separate groups. The fact that cirrhosis of the liver supervenes in the late stages does not militate against such a classification, since very good evidence has been brought forward to show that splenic disease may occasion secondary cirrhosis of the liver. Conspicuous predominance of splenic involvement from the beginning warrants the separate classification of such cases even when some evidence of cirrhosis of the liver is an early feature.

It would be hopeless in the present state of knowledge to attempt a classification of all of the cases that have been reported. On the other hand, it is very evident that there are very different sorts of cases that have more or less superficial resemblance, and I cannot share the view that all are probably instances of one disease in different stages. The ultimate solution of the matter must, seemingly, come from more careful clinical and pathological study of these cases, with recognition of the fact that the long continuance of the disease may cause very different lesions at different stages. The following varieties may be recognized provisionally:

1. *Simple Splenomegaly.* In a certain number of cases, including some described by Müller, Banti, Osler, Rendu, Peter, Sippy, and others, the conspicuous feature in the clinical history is the splenic enlargement. Anæmia is not by any means an invariable symptom, though usually present, especially when hemorrhages occur. The hemorrhages may be a purely splenic feature in the sense that they are caused by mechanical obstructions brought about by traction on the splenic vein, or they may be caused by general conditions less readily explained, as, for example, in the case of hemorrhages from the gums. Pathologically speaking, this variety belongs in the category of chronic splenitis such as occurs secondary to malaria, syphilis, rickets, and chronic gastrointestinal diseases. The lesion is essentially a fibrous hyperplasia. In some instances the endothelial cells of the sinuses are swollen and large macrophages are found; in others these cells are not observed, possibly on account of the late stage at which the disease has terminated. Analogy suggests that some form of chronic infection or intoxication is the

cause of this variety. The tendency to some endothelial proliferation does not exclude this view, for in all kinds of chronic splenitis such endothelial processes may occur. In some cases the disease may persist for a long time and the patient may ultimately die without additional lesions; in other cases changes in the liver develop as a final stage and cause a marked alteration in the clinical features. These latter cases are, I believe, in some sort different from the former in their pathology, and may for convenience be separately classed as

2. *Simple Splenomegaly Terminating in Cirrhosis of the Liver.* Perhaps the cases which ultimately develop cirrhosis of the liver and assume the fully developed character of Banti's disease are cases which from the start had a prominent grade of endothelial proliferation in the splenic sinuses. Banti has shown that there may be an endophlebitis extending from the spleen to the splenic vein and eventually to the portal vein, and he referred the cirrhosis of the liver to this cause. In the cases recently reported by Dock and Warthin, stenosis of the portal vein was discovered, and this may have been preceded by a similar endothelial process. In one of my own cases there were, within the terminals of the portal vein in the liver, large endothelial cells corresponding to those found in the splenic sinuses and in the regional lymphatic glands. In Bovaird's case large endothelial cells corresponding with those found in the sinuses of the spleen were a conspicuous feature in the portal spaces of the liver. The probable embolical origin of these formations could not be overlooked. All of these facts suggest that cirrhosis of the liver as a termination of splenomegaly is particularly likely to occur when the process from the beginning has been inclined to affect the endothelial cells in the splenic sinuses particularly. A review of the cases reported in the literature discloses the varying degree of endothelial proliferation that may be present, and it seems likely to me that this is not the result merely of the different stages at which the examinations happened to be made, but rather the consequence of natural difference in the pathology of different cases. Even accepting this, however, the difference may be only one of degree.

That splenomegaly may actually precede cirrhosis of the liver, or at least any considerable degree of cirrhosis, was shown distinctly by one of my cases (Case V.) here reported, in which the patient had been under my observation for over a year preceding the final development of the well-known symptoms of Banti's disease. When she came under observation there was a decided enlargement of the spleen, but no other signs of illness.

3. *Splenomegaly with Marked Constitutional Disturbances.* A certain number of cases of splenomegaly have been described in which, in addition to the enlargement of the spleen, there has been a

profound disturbance of the general health, causing a stunted growth, clubbed fingers, osseous changes, and pigmentation of the skin. Gilbert and Fournier report a group of such cases in children in whom the symptoms were those enumerated, together with enlargement of the liver and jaundice. Frederick Taylor has also reported a series and refers to the case of H. R. Smith, another presented in the Medical Society of the Hospitals of Paris, and some other less certain instances. In some particulars the group of family splenomegaly described by Brill is analogous, though in other particulars more suggestive of the variety of simple splenomegaly. In considering these cases, which have for the most part been observed in young persons or children, the difficulty of distinguishing the disease from hypertrophic cirrhosis of the liver (Hanot's disease) must be kept in mind. Furthermore, pigmentation of the skin of non-icteric character may be accounted for in various ways, and in some of the reported instances the possibility of its being arsenical must be remembered, while in other cases the whole condition may belong to that uncertainly defined affection called hæmochromatosis, in which cirrhosis of the liver is often an incident. Leaving out uncertain cases, however, there seems to be a group or variety in which splenomegaly is associated with stunted growth, pigmentation of the skin, clubbing of the fingers, and other evidences of general systemic disturbances. In this group probably belong two of the cases here reported. These presented very different clinical features from those shown by other instances of so-called splenic anæmia or splenomegaly.

4. *Splenomegaly Primitive.* While it is not possible perhaps to distinguish this variety clinically, there is a sharp distinction in the pathological features. It will be recalled that the essential characteristic of this condition is the presence of irregular oval spaces surrounded with fibrous tissue, and more or less filled with large endothelial cells containing one or more nuclei. All writers agree that these alveoli are formed by the proliferation of the endothelial lining of the splenic sinuses, with fibrous hyperplasia of the surrounding tissue, causing the formation of a coarse reticulum.

Bovaird has suggested that the proliferated endothelial cells eventually form fibrous tissue, and Rolleston and Osler are disposed to admit this as a probability. Harris and Herzog dissent from this opinion. When the descriptions and figures of the cases of Gaucher, Picou and Ramond, Collier and Bovaird are examined, it may not seem impossible that the endothelial process might be the forerunner of an ordinary fibrous change; that, in other words, as Rolleston states, the endothelial proliferation may be replaced by a fibrous tissue process. When, however, the macroscopic as well as the histological features in my own case are considered, it will be seen that the transformation into the ordinary characters

of a fibrous splenitis could not have occurred after a lapse of any amount of time. From every point of view the case suggests a neoplasm. In reporting his case Bovaird considered the respective merits of the neoplasm and hyperplasia theories, and concluded that the condition was rather one of endothelial hyperplasia. He referred to the doctrine of Thoma, that a tumor must be an autonomous growth. On the other hand, all pathologists are agreed that there is no sharp dividing line between the processes which may be properly called hyperplastic and those which are strictly speaking neoplastic. In reviewing the cases of splenic anæmia in which the endothelial hyperplasia has been a feature it will be seen that there are all grades of conspicuousness of this part of the pathological processes—from those cases in which the predominating feature is a fibrous hyperplasia, with a certain element of endothelial proliferation superadded, up to those cases like my own (Case III.), in which the macroscopic features of the condition were those of a tumor and the microscopic characters those of an active neoplastic formation, essentially and primarily involving the endothelial cells.

Pathological Anatomy. Compared with the mass of clinical material the pathological data are scant and unsatisfactory. In part this is due to the chronicity of the disease and in part to the fact that the examinations have been made at various stages, when presumably diverse conditions might be expected. The most extensive of the more recent studies are those of Banti. In brief the following notes contain the results of his examinations:

The spleen is much increased, weighing from 1 to 1.5 kilograms. The shape is preserved, the surface smooth and regular. The capsule is thickened and on section the substance is dark brown and hard, showing thickened trabeculæ and whitish nodules which correspond to the Malpighian bodies.

Microscopically the Malpighian bodies were found in various stages of fibrous transformation, the process beginning around the vessel within the body. A certain amount of hyaline transformation was also apparent. The splenic pulp showed no special enlargement of the venous channels. In the earliest stage there may be found in some of the veins a lining of large cells, making the vessel appear almost like an epithelial channel on cross-section. These large cells have a limited amount of protoplasm and a large nucleus of a diameter of from 5 μ to 8 μ. The same kind of cells are found in the reticulum surrounding the veins, and in some of the channels the cells have become loosened from the walls and fill the lumen of the vessel, giving the appearance of a cancerous alveolus. In some spaces actual giant cells and occasionally cells containing normal or degenerated red corpuscles were observed. The reticulum of the pulp was evidently thickened and of hyaline

appearance. This was always a conspicuous feature and distinguished the tissue absolutely from normal spleen. The thickening of the reticulum is in proportion to the duration of the disease, and finally areas of the splenic pulp may become entirely fibrous. In view of the process of fibrous transformation and the multiplication of cells within the veins, Banti proposed the name "fibroadenia." He does not believe there is a new-formation of fibrous tissue in the ordinary sense of the term, but rather an increase of the reticulum from exudation from pre-existing cells.

The liver is reduced in size, granular, and hard. In earlier stages of the disease it may be normal in size and smooth. Microscopically there is found a marked interlobular cirrhosis like that due to alcohol.

Banti calls particular attention to sclerotic endophlebitis of the splenic vein, causing irregular thickening and sometimes even atheromatous and calcareous foci. These conditions also extend into the portal vein, and in the ascitic stage of the disease even the mesenteric veins may be affected, though in less degree than the splenic.

The bone-marrow showed all the characteristics of fetal marrow, but nucleated red corpuscles were present in small numbers.

Bacteriological examination of various tissues and the blood proved negative.

Most of the reports published since Banti's correspond in all essential details.

According to Osler[1] two conditions have been described in the spleen: (1) a fibrosis and hyperplasia with atrophy of the pulp and a hyaline degeneration of the Malpighian bodies, and with this description, according to MacCallum, Osler's cases Nos. 4, 5, and 16 correspond; (2) on the other hand, very remarkable change is found in certain cases which agree in every clinical particular with the definition of the disease as given for ordinary cases. The normal texture of the spleen is replaced by fibrous tissue and large endothelial cells with clear protoplasm containing two or more nuclei and among them giant cells. This was the condition first described by Gaucher as primary endothelioma.

Sippy[2] could find records of but ten post-mortems in which he felt reasonably certain that the cause of death was "splenic pseudoleukæmia." The liver was usually enlarged, the surface smooth, the edges rounded, and no evidence of cirrhosis, though under the microscope slight increase of the interlobular connective tissue may be found. The spleen is always increased in size, and there may be perisplenitis. Its surface is usually smooth, but sometimes peri-

[1] Transactions of the Association of American Physicians, 1902, p. 429.
[2] The American Journal of the Medical Sciences, November, 1899.

toneal adhesions have been recorded. In a case reported by Banti there was visible increase in the connective tissue, and small white areas about the size of a pea were noted, and these proved to be made up of connective tissue. In Sippy's[3] case there was no macroscopic evidence of connective tissue, but microscopically considerable fibrosis was the feature of interest. Banti summarizes the findings in the spleen as follows: (1) atrophy and sclerosis of the Malpighian corpuscles, and (2) substitution of a fibrous reticulum for the delicate reticulum of the splenic pulp. As a rule, according to Sippy, the Malpighian bodies have been found but slightly altered. In his own case a few were sclerosed, the greater number showing no change.

The following is quoted from the description of West ("A Case of Splenic Anæmia, Splenomegalie Primitive," *Medico-Chirurgical Transactions*, 1896): "The spleen showed slight increase in the trabecular tissue—*i. e.*, slight fibrosis. Malpighian corpuscles are much diminished in size and badly developed. Iron reaction negative." Kanthack examined the tissues in West's case and referred to the presence of giant cells in addition to the fibrosis.

Sippy does not quote extensively from others regarding the pathological anatomy, leaving the impression that the histology as observed by others was practically the same as given in the above.

Dock and Warthin[1] report two cases with anatomical studies. In the first the liver was small and showed a moderate increase in connective tissue, especially in one area. The spleen had a thickened capsule and showed a dense fibrous network enclosing enlarged blood spaces. . These were lined and in many cases partly filled with large endothelial or reticular cells containing one or more lightly staining nuclei, and in the majority of cases nucleoli. "The fibrous tissue represents a hyperplasia of the reticulum of the pulp, the endothelial cells lining the blood spaces apparently taking part in the formation of the new fibrous tissue."

The bone-marrow was red and contained an increased number of normoblasts and very few giant cells. The retroperitoneal glands were enlarged and of the type known as hæmal gland.

In their second case the liver was small, adherent to the diaphragm by tough adhesions, and the surface on section was granular. It was the picture of an atrophic cirrhosis on microscopic examination.

The spleen showed marked fibrosis with hyaline change of the new-formed connective tissue. This process was uniform throughout the organ. The blood spaces were lined by large hypertrophic endothelial cells. A few giant cells were found in the blood spaces,

[1] Transactions of the Association of American Physicians, 1903.

and the author suggests that these may have been embolic and of bone-marrow origin.

In both of the cases there was a stenosis of the portal vein, and as the pathological lesions are entirely compatible with chronic congestion of the spleen they suggest that the condition of the portal vein may have been the cause of the lesion.

They find nothing in recent accounts of splenic anæmia suggesting the occurrence of this condition of the portal vein, but several cases were reported by Sir Andrew Clark.[1] The lesions of the splenic and portal vein described by Banti differed somewhat from that reported by Dock and Warthin, though perhaps later stages of the conditions observed by Banti might correspond.

Williamson[2] describes a case which came to autopsy and in which the histological features were sclerosis of the Malpighian bodies, general fibrous hyperplasia, great congestion of the pulp, and sinuses filled with large corpuscles containing cells. The last-named cells contained from six to ten red corpuscles and were mononuclear. I find no other recorded case with such conspicuous macrophages. Allusion is made by some authors to occasional large endothelial cells containing red corpuscles or fragments of such, but not to the numbers found by Williamson nor to cells of the peculiar character figured by him. In a case studied by Rolleston, the spleen, weighing thirty-seven ounces, "showed fibrosis with widespread proliferation of the endothelial cells and disappearance of the leukocytic elements."

Taylor, in referring to one of his cases of "splenomegalic cirrhosis of the liver," states that "the spleen was loaded with red corpuscles; otherwise it appeared normal."

One cannot read the accounts of pathological examinations, scanty and unsatisfactory as they are, without receiving the impression that they very probably refer to different pathological conditions, however similar the clinical features. There are three sorts of changes that may be clearly distinguished: (1) congestion, (2) fibrous transformation, and (3) endothelial proliferation. The first of these was conspicuous in only a few of the cases, and is more prominent in instances (like that of Strümpell) of doubtful character. Fibrous hyperplasia of the splenic reticulum and sclerosis of the Malpighian bodies constitute a marked condition in nearly all of the cases—a fact which is, of course, easily explained by the chronicity of the disease and the late stage at which the histology has usually been studied. What the conditions might have been at earlier stages cannot be determined by such examinations. The endothelial proliferation is not

[1] Transactions of the London Pathological Society, 1867.

[2] Medical Chronicle, May, 1893.

peculiar to cases of so-called splenic anæmia. A certain amount of such proliferation is found in cases of infectious splenitis of all kinds, and this doubtless contributes, in such cases as in splenic anæmia (Bovaird, Rolleston, Osler, Dock and Warthin), to the fibrous change in the reticulum.

A very different condition is that first described by Weichselbaum as "Primary Multiple Endothelial Sarcoma of the Spleen," and later by Gaucher as "Epithelioma primitif," and by Debove and Bruhl as "Splenomegalie primitive." Among the cases of this description are those of Weichselbaum, Gaucher, Collier, Picou and Ramond, Bovaird, and my own (Case III. of this series). The case of Weichselbaum and mine differ from the others in having a more marked neoplastic appearance on macroscopic examination. The opinion of Birch-Hirschfeld that Weichselbaum's case was one of endothelial hyperplasia rather than a tumor does not accord entirely with the gross appearance of the organ, though it is more applicable to Weichselbaum's case than to my own. This will appear from the recorded description.

Weichselbaum[1] remarks, by way of preface, that he was unable to find any instance of primary sarcoma of the spleen in the literature. The specimen was obtained from the body of a soldier twenty-one years old. No clinical data are given. The spleen was "somewhat enlarged," hard, dark brown in color, and presented visible follicles. On section the surface was found studded with small nodules the size of a millet-seed or pea, grayish-red in color, rather soft, and projecting above the cut surface. Their color distinguished them sharply from the splenic tissue, but there was no other sharp demarcation. On microscopic examination there was found a fibrous reticulum, coarser than that of the normal reticulum of the spleen, but no distinct alveolar arrangement. In the meshes of the reticulum were found large endothelial cells of round, oval, or irregular shape, some of the latter having projecting processes. The nuclei were large and often double. In the periphery of the masses large cells containing remnants of red corpuscles or yellowish pigment were found. In the same region extension of the processes of the cells into the fibrous reticulum was observed. All other organs were uninvolved.

In Collier's case the involvement of the spleen was in the form of a zone of cortical infiltration, and Bovaird describes pyramidal formations of white or yellowish-white color extending deeply into the substance of the organ, and involving the greater part of its anterior half, while the posterior half was comparatively free. In Picou and Ramond's case the macroscopic appearance of the organ is not described with sufficient accuracy. In none of these cases

[1] Virchow's Archiv, 1881, vol. lxxxv. p. 563.

was the condition so similar to that of definite neoplasms as in mine. It is not impossible though difficult to conceive how in any of these cases a longer duration could have led to an effacement of the conspicuous cellular process, and a conversion by fibrous hyperplasia into an organ such as those previously described in cases of ordinary splenic anæmia. It may be admitted as probable that endothelial proliferation is a precursor of some of the fibrous-tissue formation in splenic anæmia as well as in chronic splenitis, just as the same process may lead to sclerosis in the peritoneum; but it seems to me just as unlikely that the endothelial process in the six cases under consideration could have terminated in complete fibrosis as that endotheliomata of the peritoneum may have a like conclusion.

It is always difficult to draw sharp lines between cellular hyperplasias and tumors. In the case of glandular affections of the gastro-intestinal mucosa, in certain epithelial proliferations in the liver, thyroid gland, and breast, this difficulty is well recognized. The microscopic features alone do not suffice, and an appeal must be made to the gross appearances, the etiological relations, etc. Viewed in this way, I cannot avoid the conclusion that my own case belongs in the category of tumors rather than of simple cellular hyperplasia. The peculiar prominence of giant cells naturally raised the suspicion that the process might be infectious or parasitic, but no form of bacterial organisms nor anything suggesting protozoa could be discovered.

One of the arguments advanced in opposition to the tumor theory in such cases is the preservation of normal splenic appearances. As one author states, "After all these years the organ is still a spleen." This preservation of normal appearance is, however, more superficial than real, as sections through the organ showed in several cases almost complete transformation of the splenic substance.

The conclusion to which I have come is that the cases of splenomegaly of the type of Gaucher represent a primary neoplasm of the spleen somewhat comparable to the diffuse myelomata, and to certain infiltrating sarcomata of the liver.

REVIEWS.

CLINICAL TREATISES ON THE PATHOLOGY AND THERAPY OF DISORDERS OF THE METABOLISM AND NUTRITION. Part IV. The Acid Autointoxications. Part V. Concerning the Effect of Saline Waters on Metabolism." By Prof. CARL VON NOORDEN and Dr. CARL DAPPER. New York: E. B. Treat & Co., 1904.

MOST interestingly expressed and clearly defined are the authors' views on the difficult subject of defective metabolic processes with the resultant intoxications. Acetone, formerly regarded as the cause of diabetic coma, is proven to be the least significant of the three acetone bodies: oxybutyric acid, diacetic acid, and acetone. The acetone bodies are regarded by the author as products which, under normal conditions, should have undergone further oxidation, that is, that with proper supply of oxygen they would not exist in the urine at all except as acetone in very small quantity. The appearance of β-oxybutyric acid in the urine, the undoubted cause of diabetic coma, is indicative of a very grave defect in oxidative function. The fact that the acetone bodies are non-toxic when taken by the mouth leads to the view that their effects are produced by union with the fixed alkalies of the body, and are thus poisonous because acid. Acetonuria, having been produced experimentally by starvation as well as by persistence in a meat-fat diet, and having been made to disappear by the addition of carbohydrates to the diet, the author is led to the conclusion that the acetone bodies appear solely because of lessened carbohydrate feeding. In regard to the *modus operandi* of the carbohydrates in this connection the suggestion is advanced that the influence is a contact effect, oxygen being liberated within the cell. In diabetes where the acetone bodies are excreted in quantities greater than in any other condition the cause is traced to several sources: the destruction of those cells which should aid in the disassimilation and oxidation of the bodies, the failure of combustion of even the small amounts of carbohydrate administered, and finally the small quantity of carbohydrate food actually taken. β-oxybutyric acid and diacetic acid may be made to disappear altogether in some cases of diabetes by administering certain quantities of carbohydrates, but this effect can never be produced unless some quantity of the carbohydrates undergo combustion and not all be passed unused. In such cases no benefit, but in all probability positive harm, would result from the administration of carbohydrates. von Noorden frankly points

out several apparent fallacies in this theory of the etiology of the appearance of the acetone bodies, but as the fallacies are not insuperable we can afford to accept the theories and look for further elucidation along the same lines. The therapeutic measures of combating acidosis based on the theories evolved are divided into (1) means directed to the limitation of the formation of the acetone bodies; (2) means directed toward the disintoxication of the bodies circulating through the tissues and toward accelerating their elimination. The first is employed with every hope of immediate success in non-diabetic cases. In diabetes the difficulties are much greater, and here the treatment consists in careful administration of carbohydrates until the acidosis is diminished in quantity or that happy result obtained, the disappearance of all acid. von Noorden has had great success follow his oat-meal treatment. Finally, we have the power in many cases of neutralizing the acid by free use of sodium bicarbonate and sodium citrate given daily by mouth, or intravenously as sodium carbonate, in diabetic coma.

Part V. of von Noorden's series of treatises deals with the action of saline waters on metabolism, especially in those conditions most frequently seen at watering-places. While all the patients under the care of the author are put upon rigid measured diets, yet that this alone is not responsible for the cures reported is satisfactorily shown by control experiments in which the diet was not assisted by the waters, with, in most instances, less satisfactory and less rapid improvement. The effect of the saline waters is discussed in cases of alcoholic dyspepsia, hyperacidity, subacidity, anacidity, and obesity, and its use in aiding the elimination of uric acid. The author believes that the exclusion of fruit, vinegar, salads, etc., from the diet is not based on findings of scientifically conducted experiments. There are many exceptions taken to old fetishes held sacred at certain spas. von Noorden finds that fat in large quantities is readily absorbed by patients partaking of alkaline waters, and in selected cases is of the greatest benefit in the treatment, while, on the other hand, in treating obesity where fat in the diet is restricted or altogether interdicted, the waters do not increase the proteid metabolism, and thereby weaken the patient, as has been claimed. The treatise is full of interesting information conveyed in an authoritative way. J. N. H.

EVOLUTION AND ADAPTATION. By THOMAS HUNT MORGAN, Ph.D. New York: The MacMillan Company, 1903.

THIS book, which numbers 464 pages, is arranged in the form of a critical review of the various theories and hypotheses which have been advanced for and against the doctrines of evolution and

adaptation. The subjects are treated in a scientific but free manner. Darwin's *Origin of Species* is extensively quoted from and discussed at length.

After analyzing the views brought forward by other workers, the author draws certain conclusions, which differ in many points from those of Darwin and others, especially as regards the origin of species and the importance of adaptation to environment in the determination of these species.

The book is well printed on good paper and forms altogether an interesting treatise. W. T. L.

AN INTRODUCTION TO VERTEBRATE EMBRYOLOGY, BASED ON THE STUDY OF THE FROG AND THE CHICK. By ALBERT MORSE REESE, Ph.D. With 84 illustrations. New York and London: G. P. Putnam's Sons. The Knickerbocker Press, 1904.

THIS small book presents the subject of embryology in a concise and understandable form, and, as an introduction to the study, is especially adapted to students. The development of the frog and of the chick are separately considered. The first chapter, a rather long one, follows the series of change in the growth of the frog from the ovum to the adult, while the remaining seven chapters deal with the development of the chick. In considering the development of the chick a more or less arbitrary but useful division is made, inasmuch as the stages are described in periods, the first five days taking up five chapters.

The larger treatises and text-books upon the subject have been freely consulted. The illustrations are numerous and fairly satisfactory, being adapted from other publications. As an outline for the study of embryology the book seems very valuable.

W. T. L.

TRAITE DE HEMATOLOGIE. PAR FERNAND BEZANCON ET MARCEL LABBE. Avec 125 Figures et 9 Planches en couleurs, d'apres les Aquarelles de M. Labbe. G. STEINHEIL, editeur. Paris, 1904.

THE recent studies upon leukocytogenesis and upon the origin in general of the formed elements of the blood have, among other things, emphasized the close connection which exists between the hæmopoietic organs of the cells in the circulating blood. For a proper understanding, therefore, of the alterations in the blood cells during pathological conditions some knowledge of the condition of the hæmopoietic organs must be gained, since the changes in these organs and those in the circulating blood are, after a manner, interdependent. In the present volume advantage has been taken of this fact, and a rather unusual treatment of the subject

of hæmatology produces a result that is both interesting and refreshing. The work, which is quite large, covering over 900 pages, cannot be considered in the light of a text-book for students. The technique of blood examinations is relegated to a position of minor importance, and, instead of the usual concise and hackneyed descriptions of the blood in various conditions, each element of the blood is considered separately in its relation to various systemic and local diseases, and also in its relation to the hæmopoietic organs. The book is divided into several parts. The first part deals with the general properties of the circulating blood, the bacterial and chemical analysis, while the second part takes up the technique of blood examinations. After this introduction the red blood corpuscle is considered, including a short chapter on hæmolysis. A fourth division takes up the white blood corpuscle and a fifth the hæmatoblasts. The various properties of the serum, including a chapter upon bacteriolysins, cytolysins, agglutinins, and precipitins, make up the sixth part; the seventh and last part is principally devoted to a description of the hæmopoietic organs. The beauty and excellence of the colored plates are especially to be noted.

It is to be regretted that important phases of anæmia and leukæmia are considered in rather a meagre manner compared to the elaborate treatment of the other subjects.

References to original articles are numerous, and the various sides of disputed questions are fairly well presented. In this way a vast amount of valuable data has been collected, and what is not absolutely new often seems so from the manner in which it is considered. W. T. L.

RABIES: ITS PLACE AMONG GERM DISEASES AND ITS ORIGIN IN THE ANIMAL KINGDOM. By DAVID SIME, M.D. Cambridge: The University Press, 1903.

AFTER reading Dr. Sime's book one is at a loss to know why it was written or what purpose it serves. Throughout the various chapters the author unfolds and elaborates certain hypotheses concerning the mode of transition of the disease, the character of the rabies virus, and the structure of the rabies germ, the incubation period of the disease, and the changes in preventive inoculation. The work is largely based upon the author's own interpretation of Pasteur's experiments, which are extensively quoted and turned to suit the occasion. There is profound disregard for, or perhaps ignorance of, the modern conceptions of bacteriology, while the recent investigations upon rabies receive no mention whatsoever. The greater part of the book deals with the rabies-germ, and though the author admits on page 86 that "as yet the rabies micro-organism itself has not been conclusively identified," this fact does

not deter him from picturing it in its many forms as he conceives it. Further, the book is teeming with inaccuracies and misstatements, as, for instance, on page 99, where, in speaking of the "prophylactic or non-recurrent" infections, and the "preventive or recurrent" infections, the following statement is made: "Under the first head would be comprised such *germ diseases* as smallpox, anthrax, syphilis, scarlatina, measles, whooping-cough," etc. Again one finds on page 103: "There can be no doubt that like anthrax, smallpox, syphilis, and the entire prophylactic order it (rabies) affects animals in common with man, and particularly the domestic animals." From certain foot-notes it seems possible that the book was really written several years ago. This would probably be the kindest explanation for its existence. W. T. L.

STUDIES IN HETEROGENESIS. By H. CHARLTON BASTIAN, M.A., M.D. Lond., F. R. S. With 815 illustrations and photomicrographs. London: Williams & Norgate, 1903.

IN the preface the author states that his observations admit of three interpretations: (1) "It may be said that the forms of life here described, which seem to take origin from substance of other organisms or their germs, are not alien organisms, but normal stages in the life-history of the present forms." (2) "That the resulting forms of life are due to the invasion and multiplication of parasites within what appear to be the present organisms." (3) "That the resulting forms of life are, in reality, heterogenetic products originating from the very substance of the organisms or of the germs from which they proceed."

The third interpretation is chosen, and the term heterogenesis is considered to mean "processes by which living things arise from the matter of pre-existing organisms belonging to a totally different species."

The entire book, numbering almost 400 pages, resolves itself practically into a compilation of the record of observations upon what seems to the author to be a transformation of certain lower forms of life from one species to another. But, aside from the biological questions involved, the technique of most of the experiments is not such that one would be disposed to consider the results in a very serious light.

Indeed, when one reads a chapter in the appendix "On the Great Importance from the Point of View of Medical Science of the Proof that Bacteria and their Allies are Capable of Arising *de novo*," he feels much as if he were dealing with a pre-Pasteurian treatise. W. T. L.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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On the Occurrence of Lipase in the Urine as a Result of Experimental Pancreatic Disease.—In pancreatic diseases in which fat necroses occur it is generally believed that the latter are due to the action of lipase, the fat-splitting ferment of the pancreatic secretion. It is probable that the ferment reaches the fat cells by various channels. It may become diffused by an exudate throughout the abdominal cavity; it may travel through the areolar tissue, or it may be carried in the lymph and blood currents. The great preponderance of cases in which the necroses are practically limited to the immediate neighborhood of the pancreas or to the subperitoneal fat favors the first two methods. The fact that the fat necroses have been found in the pericardial, subpleural, and subcutaneous fat of the chest and abdomen and in the intermuscular tissue and bone-marrow, suggests very strongly that, in exceptional cases, the ferment is carried in the lymph and blood stream to distant parts of the body.

HEWLETT (*Journal of Medical Research*, May, 1904, p. 377) has carried out a series of experiments on dogs with the view of determining the relation, if any, between experimental disease of the pancreas and the presence of a fat-splitting ferment in the urine. Lesions of the pancreas were produced by injecting various substances into the pancreatic duct, ligaturing the duct, etc. Without going into the details of the writer's method of determining the presence of lipase in the urine, the essential features of the test are as follows: Equal quantities of urine are poured into two flasks. The contents of one flask are boiled to destroy any ferment that may be present. Both urines are neutralized with sodium hydrate. A measured quantity of ethyl butyrate and a little toluene are added to each, the latter to prevent bacterial growth, and the flasks placed in a thermostat at 39° C. for twenty-four hours. The contents of each are then extracted with ether, and the relative acidity of the two ether extracts is determined by titrating with $\frac{N}{20}$ potassium hydrate solution. Any decided dif-

ference between the acidity of the ethereal extracts of the boiled and of the unboiled urine is due to the butyric acid formed by the cleavage of the ethyl butyrate by the lipase, and where the difference in acidity is at all marked the odor of the butyric acid can be easily recognized.

Ten dogs were operated on. At the autopsy, performed at varying periods after the operation, fat necroses were found in eight. In all these a fat-splitting ferment was demonstrated in the urine. The experimental pancreatic lesions in which lipase was found in the urine were acute pancreatitis, acute obstruction of the pancreatic duct, and pancreatic trauma. Hewlett expresses the belief that lipase is present in the urine at some time during the course of most pancreatic diseases which give rise to fat necroses. It was found in greatest amount in experimental acute hemorrhagic pancreatitis. It also occurred from three to five days after obstruction of the pancreatic duct. These are the two conditions in which fat necroses are most apt to occur in human pancreatic disease. Hewlett states that very little, if any, lipase is present in normal urine. It appears, therefore, that the finding of lipase in the urine is of considerable diagnostic importance in determining the existence of pancreatic disease.

A Contribution to the Knowledge of the Purin Bodies of Human Feces in Health and Disease.—WALKER HALL (*Journal of Pathology and Bacteriology,* March, 1904, p. 246) has conducted a series of investigations to determine the quantitative excretion of purin bodies (uric acid plus the xanthin or purin bases) in the feces, to ascertain the absorption quotients of the several purin bases, and to estimate the output of the fecal purins in morbid conditions.

The purin bodies of the feces may arise from (1) desquamation of the columnar epithelium of the alimentary canal; (2) the nucleoproteids of bacteria and leukocytes; (3) the fluids poured into the intestine by its secreting cells and by those of the pancreas. Bile has been shown not to contain any purin bodies. There is no evidence to indicate that either xanthin or uric acid are excreted from the tissues of the body into the intestines. In a few stray cases uric acid has been found in the feces, but only in minute quantities.

The research seemed to bring out one point which may modify our views regarding the diet of gouty patients. The thymus sweetbread and the pancreas sweetbread are both known to be rich in purins, the former in adenin and the latter also in adenin, and, to a larger extent, in guanin. Both these glands have been considered injurious for the gouty individual, owing to their richness in these purin or nuclein derivatives. Hall's investigations show that a very large percentage of the adenin of the thymus is not absorbed and is rapidly excreted, and that the guanin of the pancreas is incapable of increasing the urinary purin output and of exerting any injurious effects on the tissues. This is a return to the position of Luff, who, as a result of clinical experience, recommended the use of sweetbread in gout.

Walker Hall finds that the fecal purins show an average daily excretion in the same individual at different intervals and under similar circumstances, the quantity ranging from 0.01 to 0.03 gm. of purin nitrogen on a mixed diet. The addition of medium quantities of meat and hypoxanthin do not alter the normal amount, and they are, therefore, probably fully absorbed. When excessive amounts of meat,

thymus glands, or guanin are added to a mixed diet a large proportion of their purin nitrogen is excreted in the feces within the following twenty-four hours. The increase is due to an increase in the guanin and adenin constituents respectively. The xanthins are slightly increased, but this is probably due to oxidation processes. The fecal purins are increased in diarrhœa. He states that the prescribing of sweetbreads to patients, the subjects of metabolic disorders, seems justified by the results of his investigations, which, however, indicate that foods containing hypoxanthin and xanthin should be limited.

Walker Hall's investigation is of much interest and importance to those carrying on metabolism investigations.

SURGERY.

UNDER THE CHARGE OF

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Rhythmical Traction of the Neck for Respiratory Syncope Due to Anæsthesia.—DEPAGE (*Jour. de Chir. et Annales de la Soc. Belge de Chir.*, January, 1904) states that the rhythmical tractions of the neck have exactly the same effect as the rhythmical tractions of the tongue. The manœuvre consists in standing behind the head of the patient and then stretching the neck backward and forward twenty or thirty times a minute. This method is to be preferred to traction of the tongue for the following reasons: 1. It is easier. 2. It requires no special apparatus, such as mouth-gag or tongue-forceps. 3. It does not cause a wound. 4. It may be done by the anæsthetist without assistance by the operator.

The Leukocyte Count in Appendicitis.—HEAD (*Northwestern Lancet*, February 15, 1904) states that in a recent article in the *Münchener med. Woch.*, Rehn observes after a study of 19 cases that this procedure is of no value in the diagnosis nor prognosis of the disease. Head, after a careful study of 30 cases, states that these conclusions are too sweeping and do not express the truth of the matter, and the following conclusions are more nearly correct: The white blood count will *not* be of service in determining (*a*) whether perforation is or is not present; (*b*) whether perforation is about to take place; (*c*) whether the appendix is gangrenous or not; (*d*) whether peritonitis complicates the appendicitis; (*e*) whether the patient will or will not recover without operation.

The white blood count will determine (*a*) whether the appendicitis

is catarrhal or suppurative in the majority of cases; (*b*) whether the inflammatory process is spreading or not; (*c*) whether the disease is appendicitis or typhoid fever with appendical symptoms; (*d*) whether the disease is appendicitis or acute abdominal pain from renal calculus, gallstones, gastric ulcer, acute nephritis, acute obstruction, etc.

The laboratory procedures should be regarded as merely aids to diagnosis and not as infallible evidence for or against a certain diagnosis. They should never be studied apart from the symptoms presented by the patient and often require a special interpretation by someone familiar with the modifications of the test produced, oftentimes by the same disease at its various stages and under varied conditions.

Atrophic Cirrhosis of the Liver, Ascites, Omentofixation; Recovery after Two Years.—JONNESCO (*Bull. et Mém. de la Soc. de Chir. de Bucarest*, 1904, No. 6) reports the case of a man, aged sixty-eight years, whose condition was most grave at the time of operation, but who now, two years later, has had no return of the ascites and is apparently well. The operative procedure consisted in a double omentofixation, one intraperitoneal and the other interhepato-diaphragmatic. In order to do this the omentum was separated into two halves, one half was fixed in the sheath of the muscle on the right side, while the other was fixed by sutures against the convex face of the liver, which had previously been scarified, and the diaphragm.

Two Cases of Cysts of the Knee.—PATEL and VIANNAY (*Revue d'orthopédie*, 1903, No. 4), after reporting two cases in detail, state, in conclusion, that there exists on the internal aspect of the knee, in the region of the internal tuberosity of the tibia, between the internal surface of the superficial fascia and the external surface of the aponeurosis, a space which in four out of every fifteen cases is a true serous bursa analogous to the prepatellar bursa. There may exist isolated cysts developed in the bursa of the tendon of the semimembranosus and tending to invade the common bursa. On the internal surface of the knee, in the region of the tuberosity of the tibia, between the cellular subcutaneous tissues and the aponeurosis of the leg, one finds occasionally a serous bursa which may become enlarged as the result of traumatism.

THERAPEUTICS.

UNDER THE CHARGE OF

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Yersin's Serum in Bubonic Plague.—DR. LOUIS CAIRUS, after an experience with this serum, states that in it we have an agent of great therapeutic value in the treatment of bubonic plague; that its action is not only bactericidal, but antitoxic as well; that this double action is most efficacious when it is administered early in the disease, and is

injected both intravenously and into the substance of the buboes; that in light cases, perhaps, subcutaneous injection alone is sufficient, but in severe infections the combined method is necessary. In these latter the beginning dosage should be from four and a half to nine ounces, the intravenous dosage to be regulated according to the severity of the constitutional symptoms.—*Therapeutische Monatshefte*, 1904, No. 5, p. 221.

Antistreptococcic Serum in Acute and Chronic Rheumatism.—M. MENZER has treated with his antistreptococcic serum forty-seven patients affected with acute articular rheumatism, all of whom recovered without passing into the chronic stage. From one to two years have passed since the treatment, and no recurrences have taken place. In nine patients who had gone on to the chronic stage of the disease the treatment succeeded completely in seven, while considerable amelioration took place in the other two. In eight of these cases the results achieved have been permanent. In two other analogous cases, complicated by polyneuritis, one cure and one amelioration have taken place. Of eleven chronic cases five were cured, two much improved, and four were unaffected. Of the seven in which favorable results were achieved, five have been followed, and there has been no relapse. Of thirty-four subjects affected for the first time with acute rheumatism and treated by the serum, only one has a valvular heart lesion, and of the total number of forty-seven cases treated in only two has cardiac involvement been observed.—*La Semaine Médicale*, 1904, No. 18, p. 142.

A New Antidysenteric Serum.—DR. ROSENTHAL has elaborated a serum, by immunizing horses against the toxin of dysentery, which he used during an epidemic in the fall of 1903. One hundred and fifty-seven cases were treated, in forty of which the bacillus of dysentery was sought and found. Each patient received from five drachms to four and one-half ounces of the serum subcutaneously. The injection was painless, but in 13 per cent. of the cases was followed by an erythema; in four cases by urticaria; by arthralgia in two cases. There were eight deaths, three of which were due to other infections. All the patients entered the hospital after having been ill for a week or less, and were in the later stages of the disease. The mortality was 4½ per cent., as against from 12 to 17 per cent. in cases not treated by the serum. The serum caused all the symptoms to improve; within twenty-four hours the tenesmus diminished, the stools became fewer, and the blood disappeared. Rarely did a patient go on to the chronic stage of the infection. When the serum was used within three days of the inception of the disease recovery was established in from one to three days.—*Deutsche medizinische Wochenschrift*, 1904, No. 19, p. 691.

The Roentgen Rays in Splenic Leukæmia.—M. M. GUILLOZ and SPILLMAN have treated a girl, aged seventeen years, afflicted with disease, who had shown symptoms for two years. The rays were applied only to the splenic area, and the treatments were given for five minutes every three or four days. After each series of four or five applications a diminution of the leukocytes and of the volume of the spleen was

noticed, and the patient's general condition improved. Epistaxis, which had been a feature of the case, ceased. From the results achieved it may be observed that the Roentgen rays are able to affect deep tissues without causing superficial lesions, and that this action may be utilized to diminish the number of white blood cells in cases of leukæmia.—*La Semaine Médicale*, 1904, No. 22, p. 174.

Red Light in Noma.—Dr. W. O. Motschan reports a case of this serious affection in a boy aged nine years. The inflammation had gone on to perforation of the cheek and lip before treatment was begun, but after three days of exposure to the light of a sixteen candle-power incandescent lamp with red glass and fitted with a conical reflector, the pain ceased and the patient could freely open his mouth. Removing the lamp caused a return of the pain. Soon the secretion of the ulcer became diminished, and healthy granulations appeared upon its floor. The lesion progressively healed, until finally a small sequestrum from the mandible came away, and less than three months after the institution of the treatment there remained only a small rose-colored scar. The distance of the lamp from the ulcerating surface was about eight inches, and the exposure was continuous day and night.—*Wiener klinisch therapeutische Wochenschrift*, 1904, Nos. 21 und 22, pp. 575 and 606.

Injections of Soluble Mercury in Syphilis Neonatorum.—MM. Schwab and Levy-Bing advise this treatment on account of its lack of danger and its rapidity and efficacy. It is applicable in grave cases with visceral involvement. It does not disturb digestion and is free from the inaccuracy of the method by inunctions. The authors use an aqueous solution of the biniodide, the minimum daily dose being 0.015 to 0.03 grain for a child weighing from five to seven pounds. A series of ten or fifteen injections are given, and after an interval of two weeks a second series is administered. The treatment is to be continued at intervals in this manner. The following formula is employed: mercury biniodide, 0.05 part; sodium iodide, 0.05 part; aqua destillata, 10 parts. The solution is injected deeply into the muscular tissue, and is not likely to cause irritation.—*Journal de Médecine de Paris*, 1904, No. 19, p. 186.

Adrenalin in Hemorrhoids—Dr. M. Demay de Certant recommends as an application to prolapsed hemorrhoids cocaine hydrochlorate, one-twentieth of a grain; adrenalin, 1:1000, thirty drops; water, one ounce. The anal region should be cleansed and a pledget of cotton saturated with the above solution applied and held in place by means of a rubber dressing. The application should be renewed every three hours, until the pain has ceased. Under the influence of the adrenalin the congestion diminishes, the hemorrhage stops, the pain ceases, and the tumors become reducible. In cases of internal hemorrhoids an ointment of cocaine hydrochlorate, one-twentieth of a grain; adrenalin, thirty drops; vaselin, one-half ounce, will be found efficacious. Suppositories of like composition act well, but are likely to cause a painful defecation. While this treatment is slow in action it is sure and lasting in its effects.—*Journal de Médecine de Bordeaux*, 1904, No. 20, p. 352.

The Iodides in Cardiac Conditions.—M. LEFEVRE believes that the iodides are indispensable in organic heart disease, and that their administration should be continued for considerable periods of time in connection with some heart tonic, such as sparteine. The author's observations show that such medication continued for several years may cause the signs of simple endocarditis to disappear. He considers potassium iodide preferable to sodium iodide, since it is more active and less likely to produce toxic effects. The iodide is given twenty days in the month in dosage of five to eight grains daily. During the other ten days one-half to one grain of sparteine is given. This drug is not cumulative, is easily eliminated by the kidneys, does not disturb digestion, and may be continued for a long period after the cardiac symptoms have disappeared.—*Journal de Médecine de Paris*, 1904, No. 20, p. 199.

Diuresis by Reduction of the Ingested Fluids.—MM. HUCHARD and FIESSINGER believe that this procedure is useful in cases of dilated heart where the œdema increases in spite of digitalis and milk diet, as well as in obesity. In the cardiac cases the fluid taken should be reduced to three pints daily—water, one-third; milk, two-thirds—with a glass or two of red wine. Within two days a diuresis is set up, which lasts two, three, or more days, with abundant elimination of the chlorides. This method does not act upon the heart itself, but lessens the work of that organ, and under the reduction of fluids small doses of digitalin, large doses of which had no effect previously, act most favorably. On the second and third days of the reduction four grains of caffeine are given, and the treatment is completed by prescribing a diet of milk and vegetables, from which chlorides are excluded as far as possible, and the administration of seven and one-half grains of theobromine three times a day.—*Journal des Praticiens*, 1904, No. 19, p. 297.

Methods of Using Collargol.—E. DESANTI suggests the following: For inunctions collargol may be mixed with simple cerate in the proportions of 15 to 100, or it may be added to an equal amount of lanolin and mixed with benzoinated lard in the proportion of 30:100. One-half to one drachm may be rubbed into the skin three times a day. A healthy part of the skin should be chosen, and one richly supplied with lymphatics. The part should be cleansed with soap, water, and alcohol, and the inunction should last at least one-half hour—better one hour—and then, in order to insure complete absorption, the skin should be covered with an impermeable dressing. Intravenously or hyperdermically, collargol may be given in 1½ or 2 per cent. aqueous solution, the adult dose being from one-half to two and one-half drachms. Schmidt has injected intravenously one-half to one drachm of a 5 per cent. solution, with no bad results. He uses a hypodermic syringe plunged directly into a superficial vein. In digestive disturbances collargol may be given by mouth in solution or in pill form. Two to five coffeespoonfuls of a solution (collargol, five parts; albumin, one part; water, one hundred parts) may be given. The so-called Credé's pill consists of collargol, fifteen grains; milk-sugar, one hundred and fifty grains; glycerin, q. s. to make one hundred pills; dose, two to six daily. This agent may also be used in surgery as an irrigation

in strength of 1:1000; as a soluble urethral bougie, of 2 per cent. strength, and as a rectal or vaginal suppository, three-quarters of a grain to each suppository.—*Revue Francaise de Médecine et de Chirurgie*, 1904, No. 21, p. 501.

OBSTETRICS.

UNDER THE CHARGE OF

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Puerperal Eclampsia Twice in the Same Patient.—In the *British Medical Journal*, June 25, 1904, McCann reports the case of a patient in her second pregnancy, whom he saw at seven months with highly albuminous urine and beginning labor with partial dilatation. She was soon delivered of a stillborn child. After delivery the patient had a most severe convulsion, from which she seemed to have died. Under vigorous stimulation she gradually rallied, and finally made a good recovery.

The year previously, in her first pregnancy, this patient had eclampsia, and labor was induced at the sixth month. She had prolonged convalescence, with very slow return to health. In the present pregnancy she had been upon a restricted diet and had seemed in good health.

Intrauterine Infection of the Fœtus in Variola.—In the *British Medical Journal*, June 25, 1904, Cowie and Forbes, of the Health Department of Manchester, report three cases in which newborn children were seized with variola so soon after birth that the infection must have been received within the uterus. In spite of immediate vaccination the cases proved fatal. It is estimated that in one case infection occurred two or four days before birth; in another, seven days before birth, and in the third seven days before birth.

The case of a patient in the seventh month of pregnancy attacked by variola is also reported. She was discharged from the hospital a month after admission. A month later her child was born, showed no signs of variola, and was successfully vaccinated. In another case a five-months' fœtus was expelled in the fourth week of the mother's variola, and showed no signs whatever of the infection.

Eclampsia Treated by Thyroid Extract.—Sturmer (*Journal of Obstetrics of the British Empire*, June, 1904) describes 41 cases of eclampsia in the Government Hospital at Madras, India, treated by thyroid extract. These patients were given ten grains of thyroid extract as soon as admitted to the hospital, and five grains every four hours afterward. If the secretion of urine were scanty, saline injections were given, and hypodermic injections of morphine, one-half grain, were

also used if indicated. Under this treatment the mortality was 12.2 per cent. Saline injections did not cause increase in the urine until twenty-four hours after the beginning of treatment, while the hypodermics of morphine caused the child to be somnolent and to breathe badly.

Other treatment, in a series of 369 cases, gave a mortality of 28.7 per cent. The mortality under the use of thyroid extract, morphine, and saline injections was the lowest obtained in this hospital.

Separate Existence in the Child.—ATKINSON (*Journal of Obstetrics of the British Empire*, June, 1904) discusses the question of the exact status of the fœtus as regards its existence as a living being. The separate true existence of the child commences with the isolation of its circulation. This is brought about by the establishment of respiration or by the shrinking of the placental site in the mother's uterus. The child may attain complete independence of the mother before partial birth. There may be a brief intramaternal phase of existence when the child has a separate physiological existence, but is not legally considered a separate individual. The laws of most countries do not recognize infanticide until the child has been expelled from the body of the mother. The death of the fœtus resulting from injury during labor is commonly ascribed to the accidents of labor.

A Case of Quintuplets.—NIJHOFF reports in the *Zentralblatt für Gynäkologie*, 1904, No. 23, a case of the birth of five children. The mother was a healthy woman, aged thirty-four years, who seven years previously had given birth to a healthy male child. She had an abortion six months before the multiple birth. During her pregnancy the patient was well, but the abdomen increased rapidly in size. During a portion of the time there was a discharge of blood and clear serous fluid. In the sixth month of the pregnancy the five fœtuses and placenta were expelled during an hour's time. The first and second children were girls, the third a boy, and the fourth and fifth girls. Before the birth of the first and third children an amniotic sac presented. The first child was born in first position, vertex presentation; the second in footling presentation; the third in second position, vertex presentation; the fourth and fifth in footling presentation, with but partial extension of the feet. The placenta was readily expelled fifteen minutes after the birth of the children by gentle pressure on the fundus uteri. There was considerable uterine hemorrhage during the labor, and clots were passed freely during the puerperal period. Aside from this the patient's recovery was uneventful.

There was but one placenta, divided into three portions of unequal size. The two smaller portions belonged to the third and fourth children each, the septa being composed of amnion and chorion. The remaining greatest portion gave nourishment to the first, second, and fifth children. The septa between these children were composed of amnion only, the umbilical cords anastomosed. The first, second, and fifth children were triplets; the third and fourth were duovular twins.

The mother of the patient had given birth to twins, and other relatives had given birth to twins and triplets. In thirty collected cases it was found that birth usually occurred from the fourth to the sixth

month. The accounts of the placentæ in the different cases vary greatly in clearness and accuracy. In the John Hunter Museum, in London, is preserved a specimen of quintuplet pregnancy, and in the Kennedy Museum, in Dublin, there is a specimen of five children. It is not known that a permanent preparation of the placenta of quintuplet pregnancy is in existence.

Psychosis during Pregnancy Rendering Abortion Necessary.—TREUB (*Zentralblatt für Gynäkologie*, 1904, No. 23) reports the case of a woman, aged thirty-one years, who had had one severe labor followed by normal birth. In her fourth pregnancy she became convinced that the child would be a monster, and she had been greatly frightened by reading a novel which described such a birth. She endeavored to throw herself under a railway train, and tried to kill the monster by introducing a pin through the abdomen. She was admitted to the hospital, and every effort made to overcome the delusion, but without success. It was necessary to empty the uterus, when the patient immediately recovered.

Cæsarean Section in Eclampsia.—In a recent paper before the Edinburgh Obstetrical Society, CROOM (*British Medical Journal*, June 18, 1904) reported two cases in which he had performed Cæsarean section for eclampsia, and reviewed a series of fifty-four cases in the practice of others. The maternal mortality in the series had amounted to about 50 per cent., which was due to the desperate condition of the patients at the time of operation. He believed that the uterus should be emptied in eclampsia as quickly as possible, and that Cæsarean section is the best method of accomplishing this result.

GYNECOLOGY.

UNDER THE CHARGE OF

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ASSISTED BY

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Stypticin in Gynecology.—WEISSBART (*Heilkunde*, 1903, No. 10) has met with the best results in the use of this drug in cases of subinvolution. When hemorrhage continues after stypticin has had a fair trial he infers that the uterus must contain placental remains. He would accordingly regard it as a valuable aid in differential diagnosis in cases in which there is no urgent indication for curettement.

Pathogeny of Deciduoma Malignum.—RECASENS (*Revista de med. y cir. pract.; Zentralblatt für Gyn.*, 1904, No. 18) holds that the fetal ectodermal structures possess a specific malignant character, which is usually neutralized by the secretion of the thyroid or ovary(?); when

for any reason the normal secretion of these glands is arrested, abnormal development of the fetal structures occurs.

Case of Ovarian Chorioepithelioma.—JAFFE (*Archiv für Gynäkologie*, Band lxx., Heft 3) reports a case of ovarian tumor which developed two months after the discharge of an hydatid mole. It proved to be a chorioepithelioma. The right ovary, which was as large as an apple, showed the same histological structure. In both tumors there were multiple corpus luteum cysts, a condition which has been noted by many observers to accompany molar pregnancy. The writer believes with Pick, that overproduction of corpus-luteum tissue is the principal feature in these cases, which seems to support Fraenkel's theory that there is a direct causal relation between the two conditions. The excess of corpus luteum material in the blood leads to an increase of trophoblasts, and hence the chorioepithelial development in the uterus.

The Permanent Results of Operations for Prolapsus.—JACOBY (*Ibid.*) reports 257 cases from the Breslau and Asch's private clinics, in 200 of which the patients were kept under observation. In most of these Alexander's operation or vaginofixation was combined with plastic operations. Of the latter class 81 per cent. were cured; of the former, 95 per cent. Vaginal extirpation was performed thirty-five times with 89 per cent. of cures in 27 patients who were examined subsequently.

Prolapsus Uteri in the Newborn—BURGER (*Zentralblatt für Gynäkologie*, 1904, No. 19) reports the case of an infant who was born with a complete procidentia, which was attributed to a peculiar atrophic condition of the pelvic floor muscles, as well as those of the back and lower limbs. The infant had knock-knee and spina bifida, with the congenital deformities.

Function of the Corpus Luteum.—FRAENKEL (*Zentralblatt für Gynäkologie*, 1904, No. 19) in an interesting communication on this subject combats some of the former theories, asserting that he has frequently removed corpora lutea from both ovaries in animals, and has even cauterized the wounds, without interrupting pregnancy. He has also repeated Mandl's experiments without pregnancy resulting. He believes that corpus luteum extract has exactly the opposite action to oöphorin, and offers a better prospect of cure of osteomalacia than castration.

Ovarian Hemorrhage—BURGER (*Zeitschrift für Geb. u. Gyn.*, Band li., Heft 2) reports the case of a nullipara, aged thirty-seven years, married for nine years, who presented all the evidences of profuse internal hemorrhage. On opening the abdomen the left ovary was found to be as large as a hen's egg, the right adnexa being normal. About two litres of fluid blood were found in the cavity. On the posterior and lower border of the ovary was a ruptured cyst, the interior of which presented a smooth surface. The ovary was generally cystic. The most careful microscopic examination revealed no evidence of ectopic gestation. A corpus luteum was present, surrounded by dilated capillaries. It was inferred that the hemorrhage was due to rupture

of some of the enlarged vessels in the wall of a corpus luteum cyst. [We recall a similar fatal case reported by Dr. Boldt, and still others in the literature. If we mistake not, excessive sexual excitement and coitus near or during the time of menstruation was held to be responsible for the accident.—H. C. C.]

Relation of Movable Kidney to Pelvic Troubles.—LEBAR (*La Gynècologie*, 1903, No. 8) found movable kidneys in 28 per cent. of 1824 patients examined with reference to this condition; 375 were right-sided, 11 on the left side, and only 4 double. The writer attributes this disparity to pressure of the liver on the right kidney, especially as the result of tight lacing, aside from the normally lower position of the right and the absence of the aponeurotic band described by Zuckerkandl on the left kidney. He believes that asthenia is the main cause of mobile kidney, hence that it has no direct relation to pelvic disorders, except as these impair the general muscular tone. [We think that it is high time that this condition is recognized as the evidence more often of general enteroptosis than a surgical condition *per se*. To treat gynecological troubles, such as prolapse of the uterus and ovaries, by performing nephropexy is generally to "put the cart before the horse." —H. C. C.]

Malignant Uterine Myoma.—STROGANOWA (*Monatsschrift für Geb. und Gyn.*, Band xviii., Heft 3 and 4) presents a paper with this title, based on twelve cases. He believes that the neoplasm is not so rare as has been supposed, having usually been mistaken for sarcoma. Rapid recurrence and metastasis prove its malignancy. It originates in the muscle cells, which degenerate and bear a close resemblance to those of sarcoma. Polymorphism and granular degeneration of the cells are the characteristic appearances under the microscope.

Such tumors are originally pure myomata, rarely fibromyomata, and should always be regarded with suspicion when they grow rapidly. [If seems as if the writer had hardly substantiated his claims that these growths are not really spindle-celled sarcomata.—H. C. C.]

Hysterectomy in Puerperal Sepsis.—ASCH (*Monatsschrift für Geb. und Gyn.*, Band xviii., Hefte 3 und 4) holds that the indications for a radical operation are exceedingly uncertain. Two points are to be considered, the character and site of the infection. The difficult point to determine is whether the streptococcic infection is localized, or has already become general. If the lymphatics are involved hysterectomy should be deferred until the result of incision and drainage of abscesses has been noted. If the veins are already thrombotic it is necessary to remove them, as well as the uterus and ovaries, the abdominal route being usually preferable. The writer reports ten cases, three of which terminated fatally, while one patient committed suicide. The other six made a good recovery.

Immediate Repair of Injuries to the Pelvic Floor.—SCHATZ (*Münch. med. Wochenschr.*, 1903, No. 44) calls attention to the fact that in forceps extractions the levator ani is apt to be torn anteriorly at its attachments to the pubic bone, and that this fact should be borne in mind in introducing the sutures—a procedure which he admits is exceedingly

difficult. It is practically impossible, when a deep tear in the posterior wall is also present, to reattach the levator to the periosteum at its original site.

The writer makes it a practice when he anticipates such an anterior tear to make a deep paraproctal incision half-way up the vagina. Even if this tear is extended it can be satisfactorily sutured.

Combined Cancer and Tuberculosis of the Ovary.—GLOCKNER (*Zentralblatt für Gynäkologie*, 1904, No. 21) reports the following unique case: A girl, aged twenty years, entered the hospital with an abdominal tumor and preliminary tuberculosis, with septic symptoms. On section a solid tumor of the ovary was removed, which presented microscopically the ordinary appearances of medullary carcinoma, but the stroma contained typical tubercular nodules and giant-cells. The opposite ovary showed many tubercles and cheesy foci. The peritoneum was absolutely free from cancerous or tubercular infiltration. The patient made a good recovery, and survived the operation nearly two years, dying of exhaustion.

The writer calls attention to the interesting fact that while three cases of primary tuberculosis of the ovary have been reported by Williams and Wolff, and that he himself has met with thirteen cases of secondary tubercular infection of ovarian cysts, there is no record of any instance in which cancer and tuberculosis were found together in an ovarian tumor.

Treatment of Hæmatocele.—ZWEIFEL (*Münchener med. Wochenschrift*, 1903, No. 34) points out the frequency of encysted hæmatoceles as compared with extensive primary intraperitoneal hemorrhages, especially from tubal ulcerations. He believes that these should be treated expectantly, though the surgeon should always be prepared for secondary rupture during the first two or three weeks. After this time the only indications for interference are unbearable pain, unusual size of the blood tumor, and infection. Vaginal section is the preferable operation, care being exercised to remove the ovum and by no means to break through into the peritoneal cavity. Under this expectant treatment patients have made an excellent recovery, and have even become pregnant subsequently.

The Relation of Fibromyoma to Cardiac Lesions.—FLECK (*Archiv für Gynäkologie*, Band lxxi., Heft 1) from a study of the material at Runge's clinic found 40.9 per cent. of cardiac diseases among 325 patients with fibroid tumors, and believes that this percentage is too small, as many affections of the cardiac muscles are hard to recognize. He infers that loss of blood is not a prominent etiological factor, since only 34.6 per cent. of cardiac cases were noted in 133 in which there was no hemorrhage. In 11 autopsies brain atrophy was noted in 8 and fatty degeneration in 3. The fact that the ovaries are so commonly affected in connection with fibroid uteri, and that excess of adipose is often observed, leads to the inference that these associated conditions may be potent, the disturbance of the "internal secretion" causing the setting free of toxins which act on the heart muscle. [While attention has been frequently called to the association of heart disease and uterine fibroid, it seems peculiar that the mortality after hystero-

myomectomy is so low, though it must be admitted that the factor of "cardiac failure" after this operation is one to be taken into account, especially in stout, flabby subjects.—H. C. C.]

OTOLOGY.

UNDER THE CHARGE OF

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The Influence of the Radical Mastoid Operation upon the Hearing.—DR. EDWARD BUHE (*Archiv für Ohrenheilkunde*, Band lvi., Hefte 3 und 4) reports from Schwartze's clinic the functional results of the radical operation in 103 cases. Of these 103 cases, 35 were improved in hearing, 37 remained the same as before the operation, and 31 were made worse. Per centum thus is: improved, 34 per cent.; remaining the same, 36 per cent.; made worse, 30 per cent. The whispered voice, that produced with the residue of air in the lungs after expiration, of a strength audible to an individual with normal hearing, 6 to 7 m., was used in testing the hearing in these cases.

From an analysis of these cases Buhe concludes:

1. The hearing after a radical operation will be found to be improved or remain the same when the labyrinth and labyrinth wall are intact, the hearing for the whispered voice before operation being less than 1 m.

2. The hearing will be improved when there is before the operation an obstruction which wholly occludes the external auditory canal.

3. The hearing will be improved or remain the same if before operation the labyrinth or labyrinth wall, or both, are diseased, there being before the operation only a small remnant of hearing.

4. There will be a decrease in the hearing when before operation the whispered voice is heard over 1 m.

5. Moreover, there will be a decrease in the hearing when the labyrinth or labyrinth wall, or both, are diseased, the hearing before operation being for whispered voice more than 0.25 m. and under 1 m.

Investigations in Regard to Caries of the Ossicles.—SCHULTZE (*Archiv für Ohrenheilkunde*, Band lx., Hefte 3 und 4) reports in detail the histological appearances of the ossicles removed from twenty-four patients. With one exception the ossicles were obtained by the radical operation. Twenty-two hammers and seventeen anvils were examined. In ten cases cholesteatomata were found in the middle ear, and in fourteen cases there were caries and granulation formation in the middle ear. The appearance of the membrana tympani before the

operation of these cases supported the truth of the diagnostic sign first brought out by Schwartze, that the site of the perforation in the upper segment of the membrana points to incus or malleus caries. The size of the perforation in the membrana gives no clue to the amount of destruction which the ossicles have suffered.

Schultze divides the pathological changes which the ossicles exhibit into two classes. In cases of the first class the diseased portion of the ossicles is on the surface and uncovered. In cases of the second class the bone change is observed beneath more or less pathologically changed tissue. In both classes the pathological process is lacunar absorption, and the covering of the carious portion with granulations, polypi, or epidermis is simply an accompaniment of the process. That the caries may come about with intact periosteum the author doubts, although the caries may start at the surface as a small point, and, as the process extends more deeply into the substance of the bone, it may become larger, and connected with the surface only by a narrow tract. The occurrence of primary osteomyelitis of the ossicles the author considers unverified. The caries is practically always secondary to a periostitis, the result of middle-ear suppuration. Loss of substance, however, may be due to pressure, as has been observed on the malleus head, where a very retracted drum membrane causes the head to press on the bony wall of the attic.

The most important immediate factor in the causation of the caries is the influence of the retained and fetid pus bathing the ossicles. This is often, although not always, associated with cholesteatoma formation in the middle ear. The immunity of the articulating surfaces of the ossicles is probably dependent upon the greater resistance of the cartilaginous coverings of these parts of the bones.

In conclusion, the author discusses the worth of ossiculectomy, and concludes that this operation is indicated in many cases, both because it often removes the focus of suppuration, and because it allows a more adequate drainage of the middle ear. The indications for ossiculectomy are, however, sharply defined, and the operation is not indicated where there is evident, in addition to the caries of the ossicles, caries of the antrum, etc., or cholesteatoma formation. Here the total exenteration of all the middle-ear cavities is indicated. The author is not in favor of leaving the ossicles intact in performing the radical operation.

Ankylosis of the Malleoincudal Joint.—Frey (*Archiv für Ohrenheilkunde*, Band lxi., S. 234–246) reviews thirty-five cases of ankylosis of the malleoincudal joint which he found in the literature on the subject. He then gave a brief clinical and histological history of two cases:

Case I. Boy, aged eleven years, had suffered with chronic otitis media for the last five years. The drumhead, with the exception of a small upper edge, was completely destroyed. The handle of the malleus lay on the inner wall of the middle ear, and the tympanum itself was filled with granulations which also surrounded the handle of the malleus. After long conservative treatment without results the radical operation was performed. At the operation the whole middle ear, as well as the mastoid, was found to be filled with granulations and pus. The bone of the mastoid was brittle. In enlarging the middle ear the malleus and incus were firmly attached and came out together.

The histological investigation of horizontal sections through the articulation showed that the bone-marrow of both ossicles was increased. The ossicles were bound to each other by a long bridge, which ran at right angles to the plane of the joint and united with the bony substance of the ossicles. This bony bridge could be followed through about half the sections. Where the bone ceased calcification began, and deeper down there was union of the ossicles, through connective tissue, which took on thickening toward the periphery.

Case II. Man, aged twenty-one years, student, suffered for several years with a frequent recurring left-sided purulent otitis media. There was complete destruction of the drumhead and of the lower part of the handle of the malleus. There were small granulations along the malleus and protruding from the attic. The outer wall of the recessus epitympanum was partly destroyed. Before a greater operative procedure an ossiculectomy was performed, at which time the hammer was removed, and with it came the incus.

The bony substance of the joint heads was greatly reduced, due to the extraordinary enlargement of the bony canals; the vessels were also enlarged and distended. The cartilage was increased. Peripherally the periosteum of the ossicles was enormously thickened.

In the first case there was union of the two joint heads through new-formed bony substance within the joint, an intra-articular ankylosis.

The enlargement of the bony canals and the vessels in them, as well as the deposit of chalk, showed the ankylosis to be the result of inflammatory processes.

The second case comes under the head of a capsular ankylosis; here, also, the result of inflammation. Frey divides cases of ankylosis of the ossicles anatomically as follows:

1. The periarticular connective-tissue ankylosis.
2. The periarticular bony ankylosis.
3. The intra-articular bony ankylosis.
4. Mixed forms in which intra-articular as well as periarticular changes exist, through the addition of connective tissue, through calcification and new-formation of bone.

Etiology. As to the cause of these changes there is too little material to determine. In twenty-three cases there existed an inflammation. This cause is held by Schwartze, Jacobson, Blau, Politzer, and others.

It is more than doubtful if catarrhal changes in the middle ear, even of long duration and combined with chronic transformation of the mucous membrane, can cause any ankylosis of the malleoincudal joint. Most cases of ankylosis occur in chronic adhesive processes after old middle-ear inflammation.

On the subject of influence of malleoincudal ankylosis upon the function of hearing not much can be said. Normally the joint makes a very small excursion, and it is even questionable if this malleoincudal articulation can be spoken of as a true joint in this respect. In these cases there are always other changes of a severe nature combined with the ankylosis, and therefore conclusions cannot be drawn as to the importance of the mobility of this articulation.

OPHTHALMOLOGY.

UNDER THE CHARGE OF

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Hemorrhages in the Eye Present at Birth.—COBURN (*Archives of Ophthalmology*, May, 1904) has undertaken a study of this condition to ascertain if possible the cause of poor vision in certain eyes without appreciable changes in the fundus. Other observers have also reported such cases. Kenigstein, with the ophthalmoscope, found retinal hemorrhages twenty-nine times in 281 cases (about 10 per cent.). Schleich found seventy-eight eyes affected in 49 cases among 150 children, from birth to eight days old. In a week absorption had usually occurred, and only slight cloudiness of the retina remained. Bjerrum found only 3 per cent. of the cases he examined affected with retinal hemorrhages. De Vries found 11 per cent. affected in 112 cases. Of 150 newborn children examined by Montalcini from ten minutes to two days after birth, 25 per cent. had hemorrhages in the retina, 18 per cent. in both eyes.

These hemorrhages were mostly at the posterior pole of the eye. Most of these infants were in bad health. All were head presentations, and prolonged labor seemed to be a factor. These hemorrhages, occurring by diapedesis, absorb quickly, but they may often represent the origin of functional troubles.

Naumhoff examined the eyes of 47 children who had died shortly after birth, and found hemorrhages in 25 per cent. Von Hippel found hemorrhages in 10 per cent. out of 24 cases—41 per cent.

Coburn examined the eyes of 37 dead infants, either stillborn or aged up to twenty-two days. On opening the eyes the blood could often be seen with the naked eye. Hemorrhage was found in 17 cases, the retina being the chief site in all. Hemorrhage anterior to the iris is comparatively rare, having been observed but once (on the anterior surface of the iris and in the meshes of the pectinate ligament). Blood in the outer layers of the sclera was seen five times. Choroidal hemorrhage was not observed, though in one instance a detachment of the retina had evidently been caused by such. Hemorrhage into the optic nerve head was noticed four times; in the optic nerve sheath five times, and in the subhyaloid four times. The vitreous was involved only twice, though in some cases where the hemorrhage appeared to be subhyaloid only blood corpuscles were found in that structure.

A fact worthy of note is the intense congestion of the vessels and capillaries of the retina in these cases, showing that this structure is not so sparsely supplied with bloodvessels as is ordinarily supposed.

The author concludes that the probable cause of these retinal hem-

orrhages depends upon compression of the optic nerve and its central bloodvessels due to distention of the nerve sheath with cerebrospinal fluid from compression of the head during birth.

Local Anæsthesia in Eye Operations—GUTTMAN (*Archives of Ophthalmology*, May, 1904) produces anæsthesia of the conjunctiva adequate for operative treatment of trachoma, tumors of the lid, lacrymal abscess, etc., by subconjunctival injection of a solution of cocain, 1:1000 to 1:5000 after preliminary instillation of a 4 per cent. solution or a 1 per cent. solution of holocaine in the conjunctival sac. The needle of a Pravaz syringe is introduced very superficially beneath the conjunctiva of the fornix (in the case of the upper lid the cartilage is turned with roller forceps). The entire conjunctiva is raised in a wheal; the trachoma granules thus become prominent and plainly visible, and can readily be attacked with the roller forceps without the same injury to the whole conjunctiva, as occurs in the operation as ordinarily performed.

In operations on the external surface of the lids, as for tumors, chalazia, etc., it is not sufficient to infiltrate the outer skin alone, but the conjunctiva must also be infiltrated.

The technique of the method should be thoroughly mastered.

Removal of the Crystalline Lens in Sixty-three Cases of High Myopia.—SNELL (*British Medical Journal*, February 27, 1904) reports the following results: Sixty-three operations were performed on forty-four patients, all except one under forty years of age. The degree of myopia ranged from 10 to 28 D. The operation was successful in every case. In two cases detachment of the retina occurred at intervals of six months and one year following operation. The reporter observed that of 6324 myopic eyes occurring in half the number of his private patients about 5 per cent. presented a myopia of more than 10 D. The method of operation in every case consisted of preliminary needling, followed by subsequent extraction of the disintegrated lens substance.

Increased tension, which occurs at two distinct stages, first, by reason of the swollen lens, and second, when the pupil is free or nearly so of lens matter, was successfully met by paracentesis. The writer believes that within defined limits the removal of the crystalline lens for high degrees of myopia may now be regarded as a recognized and valuable method of treatment. He does not regard detachment of the retina as discrediting the method, considering that this is a danger which always menaces eyes affected with high myopia *per se*. Patients are usually extremely grateful for the relief the operation affords.

One Hundred Cases of Eye Diseases with Bacteriological Examination.—SMITH (*Yale Medical Journal*, May, 1904) reports such a series, of which the following is a summary:

Organisms were found in all but 11 cases, of which 7 were diseases of the conjunctiva, 2 of the cornea, and 2 of other structures. There were 62 cases of disease of the conjunctiva, 15 of the cornea, 11 of the lacrymal apparatus, 9 of the lids, and 8 operative cases. The gonococcus was found in 9, and the diplococcus in 5 of the conjunctival cases without the presence of other organisms. The remaining organisms found were frequently associated with other species. The pneu-

mococcus was found in 18 cases, of which 10 were conjunctival, 3 corneal, and 5 lacrymal. Koch-Weeks bacillus was found in 4 conjunctival and 1 lacrymal case. Staphylococcus albus was present in 10 conjunctival, 4 corneal, 4 lacrymal, and 1 other case. Staphylococcus aureus was found in 2 conjunctival, 5 corneal, 1 lacrymal, and 2 others. The staphylococcus epidermidis albus was found in 1 conjunctival and 2 other cases (without other organisms). The streptococcus occurred in 2 conjunctival, 2 corneal, and 5 lacrymal, and 2 other cases. The Morax-Axenfeld diplobacillus was present in 8 conjunctival, 1 corneal, and 1 lacrymal; in the two latter with other germs. The xerosis bacillus was found twenty-three times; it occurred in a great variety of conditions. The streptobacillus was found three times in conjunctival disease. Other bacilli, diplobacilli, and diplococci were found in 28 cases. In 7 the results were unsatisfactory.

Some of these findings are suggestive. Of the staphylococcus the albus was more often found in conjunctival, the aureus in corneal disease. In the lacrymal cases the streptococcus and pneumococcus predominated.

While zinc chloride in diplobacillus, and antitoxin in Klebs-Loeffler conjunctivitis are almost specifics, none is known for any other organism. (Silver surely almost deserves the name of a specific in gonorrhœal conjunctivitis.—Ed.)

Persistent Œdema of the Eyelid Due to Syphilis.—Snydacker (*Archives of Ophthalmology*, March, 1904) reports a case of redness and œdema of the left upper eyelid occurring in a mulatto, causing the lid to hang down so as to occlude the pupil entirely seven years after syphilitic infection. There was no involvement of the tarsus and no areas of nodular infiltration in the skin or subcutaneous tissue. This condition had persisted for four months. It disappeared after three weeks of antisyphilitic treatment. Other somewhat similar cases have been described. In most of these the tarsus was involved.

The author thinks that in his case a gummatous infiltration existed in the subcutaneous tissue, or a number of small confluent or non-confluent gummatous foci were present, which because of the œdema of the lid, could not be determined by palpation or perhaps a syphilitic tarsitis or gummatous infiltration of the tarsal cartilage existed of too slight a degree to be felt.

Non-inflammatory persistent œdema of the eyelid should always awaken a suspicion of syphilis.

Diffuse Sarcomata of the Uveal Tract.—Parsons (*Archives of Ophthalmology*, March, 1904) has collected thirty-one cases of this extremely rare condition first distinguished by Fuchs in 1882. These cases show no great peculiarity in sex, eye affected, or age of patient, except the first decade, in which none of them had occurred. The most conspicuous feature of the histories is the long duration of the disease in many cases, varying, as shown by the failure of vision, from seven months to ten years. There was a history of injury of or operation in seven cases. Most of the eyes were glaucomatous. In many, indeed, the eye was excised on account of absolute glaucoma, without definite evidence of intraocular growth. Early onset of glaucoma has been emphasized, but taken in connection with the prolonged history

in many cases it is not very striking. The early onset of extraocular extension is much more striking. This is often multiple.

Pathological anatomy. These growths are all characterized by their diffuse and infiltrating tendency as opposed to the formation of a definite tumor. The cytology is particularly interesting:

1. The frequency of large round or polygonal cells, often combined with spindle cells.

2. The frequency of an alveolar or plexiform arrangement, either throughout the growths, or in parts or in secondary extensions.

3. The frequency of hyaline and myxomatous degeneration, and the occasional presence of necrosis.

4. The frequency of extension along the perivascular lymph spaces, surrounding the perforating ciliary vessels and venæ vorticosæ.

These characteristics show the cells to be endothelial and the growth endotheliomata. They vary much as regards pigmentation, which is a phenomenon of no particular value in this connection. The retina was not usually detached. Parsons thinks that the essential characteristics of these growths, their diffusely infiltrating tendency, is explained by their flatness and their endothelial origin.

DERMATOLOGY.

UNDER THE CHARGE OF

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Symmetrical Cutaneous Atrophy.—J. A. Fordyce (*Journal of Cutaneous Diseases*, April, 1904) enters upon this subject very thoroughly, referring to the several well-known cases on record, and gives a case (with illustrations) of his own. The most interesting point brought out is the observation that the atrophic process, as shown by the histological examination, was plainly the result of an infiltration, and not of an idiopathic nature, the inflammatory process in the upper corium causing secondary changes in the epidermis. The alterations in the vessels' walls and the perivascular infiltration point strongly to those structures as being the primary seat of the disease. This view is strengthened by the clinical histories of such cases, the majority showing in their early stages primary vascular dilatation before the secondary atrophy was manifested.

Erythromelalgia and its Relation to Raynaud's Disease.—F. P. Weber (*Journal of Cutaneous Diseases*, February, 1904) gives a case occurring in a woman, aged twenty-six years, free from organic disease of the central nervous system and without alcoholic or arsenical neuritis. The left foot was the part mainly affected, characterized by flushing or

lividity of the toes, and pains there and also in the left foot. Moreover, there was habitual hyperæmia of the face and tongue. The point of interest in the paper is the observation that there is no distinct line separating this disease from Raynaud's disease. The early symptoms of both forms of disease are surely of nervous origin, and can best be explained on the supposition of a vasomotor disturbance due to the central nervous system. In both this disease and in chronic Raynaud's disease the muscular coats of the arteries become hypertrophied. Clinically, intermediate cases between the two diseases are often met with in literature, as Cassiner has shown in his work on vasomotor trophic neuroses, published in Berlin in 1901.

Lepra in the Sandwich Islands.—DALAND (*Journal of the American Medical Association*, November 7, 1903) is of the opinion, from his observations, that the Hawaiian is unusually susceptible to this disease. He also regards syphilis as a predisposing cause. While heredity is a factor, it is of minor importance. The disease he considers but feebly contagious and to be incurable.

On the other hand, Filaretopoulo, of Athens (*British Journal of Dermatology*, September, 1903), holds the belief that the disease is hereditary and seldom contagious, and that the treatment with mercurial injections and chaulmoogra oil, up to 300 drops daily, together with hygienic and dietetic regulations, are useful.

A Clinical and Histological Study of Folliclis.—ALEXANDER (*Archiv für Dermatologie und Syphilis*, Band lxx., Heft 1) concludes from a study of the histories of seven cases of folliclis that there is an undisputable relationship between this affection and tuberculosis. The nodules occur in crops, and are apt to recur at certain seasons of the year, sometimes returning every spring, or occurring only in the summer or winter. It is noteworthy that a considerable proportion of patients complain of joint-pains for which there is no clinically demonstrable cause. In some cases œdematous, painful infiltrations occur, which are due to the coalescence of several deeply situated nodules. While folliclis is an exquisitely chronic affection, there are considerable periods during which the patient shows nothing but scars. It is also distinguished by the multiformity of the lesions, which may at times be so insignificant as to escape the patient's attention and to be readily overlooked by the physician. A knowledge of this apparently in itself insignificant affection may be of great importance, since by its recognition we may be able to destroy a visible focus of infection which is a constant source of danger to the entire organism.

Histologically, the author distinguishes two types of the disease: a deep variety with tubercular change, and a superficial form with diffuse inflammatory infiltration—thrombophlebitis. Both arise, without doubt, through embolic processes, and certainly are due to tubercle bacillus itself.

The Relationship of Alopecia Areata to Dental Irritation.—BETTMANN (*Archiv für Dermatologie und Syphilis*, Band lxx., Heft 1) has studied thirty-three cases of alopecia areata, observed in the Heidelberg medical clinic, for the purpose of determining the correctness of Jacquet's theory concerning the dental origin of this affection. As the

result of the careful study of these cases he believes it would be a mistake to accept Jacquet's hypothesis unreservedly. In none of these thirty-three cases was it possible to demonstrate that the alopecia had been preceded by dental irritation.

Herpes Zoster Associated with a Generalized Bullous Eruption from Prolonged Administration of Arsenic.—SEQUEIRA (*British Journal of Children's Diseases*, vol. i., No. 4) reports the case of a girl, aged five years, to whom three minims of Fowler's solution were given three times a day for an attack of guttate psoriasis. After three months of this treatment pigment began to appear upon the trunk, and a month later the skin showed characteristic arsenical pigmentation. An eruption of vesicles and bullæ now appeared all over the trunk, the face and extremities being exempt, and at the same time an abundant zoster appeared in the lumbar region, on the right side. No other arsenical symptoms, such as palmar and plantar hyperkeratosis, muscular disturbances, or gastric catarrh, were noted. The herpes was followed by scarring, but the vesicles and bullæ upon the trunk left no scars. The author regarded the eruptions as arsenical in origin.

Eosin in the Treatment of Lupus.—LEDERMANN (*Archiv für Dermatologie und Syphilis*, Band lxx., Heft 1) at a meeting of the Berlin Dermatological Society held February 2, 1904, presented a patient with lupus who had been treated by applications of eosin according to the suggestion of Jesionek and Tapeiner. The applications had been made several times a day, and it was clearly apparent that the eosin had an elective action upon the lupus nodules, since not only the ulcerated surfaces but the superficial nodules showed evidences of destruction. In a case of cancroid of the skin there was also tissue destruction. It can be said that dyeing with eosin produces an effect similar to pyrogallol upon lupus nodules, but does not cause pain.

A Case of Paget's Disease of the Umbilicus.—T. COLCOTT and J. M. H. MACLEOD (*British Journal of Dermatology*, February, 1904) report a case of Paget's disease occurring in a most unusual region. The patient was a man, aged sixty-five years, who presented a rounded, eczematoid patch about two inches in diameter, occupying the umbilical region. This patch, which had been forming for about eleven years, was a brilliant red color, ulcerated, covered in spots by epithelium, and surrounded by a raised, well-marked, sharply defined border. The clinical diagnosis was confirmed by the histological examination. The changes found in the epidermis were typical of the disease, and the authors believe that the histological alterations in the epidermis in Paget's disease are characteristic and pathognomonic, whatever the region affected. No evidence of definite malignant change was found in the epidermis. The authors are not inclined to accept the view that the epidermic changes are malignant from the beginning. The histological appearances were suggestive of a chronic inflammatory process affecting the papillæ, leading to proliferation, œdema, and degeneration of the cells of the epidermis, in some respects resembling lupus erythematosus. The authors' researches shed no light upon the cause of the disease.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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Physiology of the Thyroid Gland.—KISHI (*Virchow's Arch.*, 1904, Band clxxvi. p. 260) describes a series of observations dealing with the extirpation of the thyroid gland in animals and upon the metabolism and the pathological changes in the various organs of thyroidectomized animals. From a study of the parathyroid glands after extirpation of the thyroid itself, he believes that the parathyroid is not an independent organ, but an embryonal thyroid rest, and under certain circumstances may be transformed into thyroid tissue. Dogs and cats often die after thyroid extirpation, even though the parathyroids are left intact. If the thyroid gland is normal the parathyroids are functionless, and they exert a function only when the thyroid is entirely removed or when that portion of the gland which remains is not sufficient to sustain life. When the quantity of parathyroid is equal or exceeds the quantity of thyroid necessary to sustain life a thyroidectomized animal does not die.

It was further found that in thyroidectomized animals metabolism was increased, while there was no change in control animals in which the thyroid gland had simply been exposed at operation. The amounts of nitrogen, sulphuric acid, phosphoric acid, and uric acid eliminated in the urine followed the same curves. The chloride excretion was very irregular.

The changes in the organs of the thyroidectomized animals were confined chiefly to the blood and bloodvessels. A direct result of thyroid extirpation was a decrease in hæmoglobin and red blood cells. The alterations of the other organs described by many authors was thought to be of secondary nature.

The author concludes from these studies that the thyroid is a secretory organ, and neutralizes within the gland an albumin that is injurious to the blood. This toxic substance is a variety of nucleoproteid derived from the cell nuclei of food. In the glandular cells of the thyroid an iodine containing globulin is formed, which possesses an attraction for the albumin of the toxic nucleoproteid. These two substances in combination are eliminated from the cells into the follicles as a third substance which the author calls "thyreotoxin." Thyreotoxin is split into two harmless products which gain access to the lymphatics and bloodvessels, and are thus eliminated.

Researches upon Chronic Passive Congestion of the Liver.—HART (*Ziegler's Beiträge*, 1904, Bd. xxxv. p. 303) has examined the liver in 35 cases of advanced central red atrophy. He finds constantly in this

condition thrombosis of the capillaries toward the central portion of the liver lobule. The capillary plugs are to be seen as soon as the degeneration of the liver cells makes its appearance, and the extent of the thrombosis is in direct proportion to the degeneration of the liver cells. The production of the thrombi forms a new argument in favor of Schmidt's theory concerning the relationship between fibrin coagulation and cell degeneration.

Upon the Properties and Production of Anticrotalus Venin.—FLEXNER and NAGUCHI (*Journal of Medical Research*, 1904, vol. xi. p. 363) have shown in previous studies that the severe local lesions (mainly hemorrhage and softening of the tissue) which follow injections of rattlesnake venom are produced in large part by a cytotoxin which destroys the endothelial lining of the bloodvessels. To this toxin they have given the name of hemorrhagin. Owing to the difficulty in overcoming these local effects of the venom no successful production of antitoxin for rattlesnake venom has so far been accomplished. The present work deals with a method of surmounting this difficulty. By treating the crotalus venom with dilute hydrochloric acid or iodine trichloride, the locally active principles could be transformed into toxoid substances. This modified venom, though deprived of a large part of its toxicity, still preserved its power to set up antivenin formation in the rabbit and dog. Thus, by injections of this modified venom an antivenin of considerable activity against rattlesnake venom could be procured. While the toxophore group of hemorrhagin was primarily attacked by the weak hydrochloric acid and iodine trichloride, both the toxophore and cytophilic haptophore groups were destroyed by strong hydrochloric acid and hydrochloric acid and pepsin, thus rendering the substance useless for antivenin production. Iodine trichloride destroyed both the groups in the neurotoxins and hæmolysins of cobra and daboia venoms.

Anticrotalus venin was found to be without appreciable antitoxic power over cobra and daboia venoms, and of imperfect antitoxic power over water moccason venom. This was in keeping with the different constituents of these venoms, for the first two owe their toxicity to neurotoxins and hæmolysins, the last to these principles together with hemorrhagin.

Precipitins were formed from venom along with or independent of the immunizing principles for venom, but there was no relation between the degree of protection afforded and the amount of precipitins present in the immune serum. The precipitins for the different venoms were highly though not absolutely specific.

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ACUTE LEUKÆMIA IN EARLY LIFE.

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Acute leukæmia is a comparatively rare disease in early as well as in adult life, but with modern methods in blood examinations cases are now recognized more frequently than formerly. Morse,[1] in 1898, reported a case in a four-year-old girl and gave a brief résumé of seven other cases under ten years of age collected from the literature. McCrae,[2] in 1900, reported a three-year-old boy with leukæmia, giving abstracts of thirteen cases, including Morse's. Since McCrae's article I have collected fourteen cases, brief abstracts of which follow:

Case I. (Strauss.[3])—Boy, aged thirteen months; family and personal history good. Illness began two or three weeks ago, with enlargement of the abdomen. General condition good; no digestive disturbance; no nose-bleed. Physical examination showed marked pallor, slight rickets, numerous petechiæ, teeth good, tonsils normal, chest normal, spleen much enlarged, urine negative. Continued thus for two or three days, then became worse, and died three weeks from onset.

Blood. Hæmoglobin, 25 per cent.; erythrocytes, 2,008,000; leukocytes, 208,000; lymphocytes, 97.3 per cent.; large mononuclears, 0.6 per cent.; lymphocytes varying in size. Some poikilocytosis and polychromatophilia; few normoblasts.

Case II. (Bloch and Hirschfeld.[4])—Boy, aged eight months; family and personal history unknown. For a few days had been unusually sleepy; no other symptoms. Physical examination showed marked anæmia, right-sided pneumonia, lymph glands and spleen enlarged, rickets. Under observation for a few days, then had double pneumonia, and died.

Blood. No total white count given, but proportion of whites to reds was 1 to 12. Polynuclears, 28 per cent.; myelocytes, 10.2 per cent.; small mononuclears, 27.14 per cent.; large mononuclears, 38.8 per cent.; poikilocytosis, megaloblasts, and normoblasts; eosinophiles and mast-cells rare. Duration unknown, but probably acute. Regarded as lymphatic myelogenous type; autopsy showed leukæmic changes, especially interesting on account of changes in central nervous system.

Case III. (Janeway.[5])—Boy, aged six years. Trouble began three months ago with swelling over masseters, later swelling of cervical and other glands, and marked pallor; no hemorrhage and no retinitis.

Blood. Hæmoglobin, 40 per cent.; leukocytes, 219,000; large lymphocytes, 87 per cent.; small lymphocytes, 11 per cent. Clinically, the case was chronic, but the blood was that of the acute type, and the author cites the case to show the impossibility of regarding acute lymphatic leukæmia as a separate disease.

Case IV. (Jewett.[6])—Boy, aged thirteen months, smaller and weaker of twins. Family history negative. Personal history: never robust.

March, 1900. Pale, occasional diarrhœa, malnutrition. April: Slight, irregular fever. May: Tumor in left abdomen. Never any enlargement of superficial lymph glands; never any hemorrhages.

Examination. June: Moderate emaciation, pale, spleen much enlarged, reaching to level of umbilicus.

Blood. Hæmoglobin, 30 per cent.; erythrocytes, 1,912,000; leukocytes, 21,000; lymphocytes, 87 per cent.; neutrophiles, 10.5 per cent.; eosinophiles, 1.5 per cent.; myelocytes, 1 per cent.; eight normoblasts and eight megaloblasts in 200 cells; lymphocytes of all sizes; poikilocytosis and polychromatophilia; fever marked; regarded as subacute lymphatic leukæmia. Death, June 17th. No autopsy.

Case V. (Jewett.[6])—Girl, aged seven months. Family history negative. For three months pallor, enlarged spleen, emaciation, diarrhœa, irregular fever, great weakness, enlarged glands. No hemorrhages.

Blood. Hæmoglobin, 20 per cent.; erythrocytes, 1,150,000; leukocytes, 33,000; lymphocytes, large and small, 78.6 per cent.; neutrophiles, 18.2 per cent.; eosinophiles, 1.8 per cent.; myelocytes, 1.4 per cent.; fourteen normoblasts in 500 cells. Death at eight months. Diagnosis: subacute lymphatic leukæmia. No autopsy.

Case VI. (Pollman.[7])—Girl, newly born. Family history negative. Mother's blood normal. Sickly at birth, never cried nor nursed, apathetic, petechiæ on forehead and lower limbs, later universal. At sixteen days cyanosis; liver and spleen much enlarged; cervical and inguinal glands somewhat enlarged; temperature from 38.8° to 41.5° C. Death at nineteen days.

Blood. Erythrocytes, 2,500,000; leukocytes, 312,500. No differential count, but leukocytes, almost all mononuclear, with rather a large nucleus. Autopsy: great enlargement of spleen and liver and thymus, *open ductus arteriosus.* Tricuspid endocarditis. Culture from spleen negative. Culture from heart blood showed only colony of undetermined organisms. General infiltration of tissues with leukocytes. No examination of bone-marrow. Regarded as a case of splenomedullary leukæmia, but probably was lymphocytic.

Case VII. (Stewart and Campbell.[8])—Boy, aged six years. Family history negative. Caught cold in March, 1901, never well afterward. Pallor, poor appetite.

Examination. April 1, 1901. Pale, submaxillary glands enlarged. Seen several times during April and May. Irregular temperature, nose-bleed, pain in legs. Spleen not enlarged.

Blood, May 26, 1901. Hæmoglobin, 21 per cent.; erythrocytes, 750,000. After large hemorrhages: leukocytes, 40,000; lymphocytes, 25 per cent.; polynuclears, 45 per cent.; myelocytes, 27 per cent.; eosinophiles, 3 per cent.; normoblasts fairly numerous. Death two days later.

Case VIII. (Einhorn.[9])—Girl, aged nine years. Family history not mentioned. Well until several months ago, then weakness, later diarrhœa.

Examination. Not pale, cervical and inguinal glands enlarged, spleen and liver enlarged, chest negative.

Blood. Erythrocytes, 3,360,000; leukocytes, 389,000; small lymphocytes, 48.7 per cent.; large lymphocytes, 49 per cent.; mononuclears, 1.3 per cent.; polynuclears, 1 per cent. No further history given.

Case IX. (Rocaz.[10])—Boy, aged four years. Came to hospital with tonsillitis, no diphtheria bacilli. Family history good. Previous history: subject to sore-throat. May 25, 1901, ill three days with tonsillitis, which subsided, but temperature remained high. In two days fetid diarrhœa.

Examination. Chest normal, tonsils enlarged, spleen enlarged. Widal reaction positive; case therefore regarded as typhoid. Four days later cervical and inguinal glands enlarged.

Blood. Hæmoglobin, 30 per cent.; erythrocytes, 1,816,000; leukocytes, 244,000; lymphocytes, 96.6 per cent.; large mononuclears, 0.6 per cent.; transitional, 0.6 per cent.; polynuclears, 2.4 per cent. Some poikilocytosis, later petechiæ, bleeding of gums. Death twenty-seven days after onset. Autopsy: hypertrophied thymus, infiltration of tissues generally with small cells.

Case X. (Fowler.[11])—Girl, aged five years. Family history good. Previous history: measles, whooping-cough, chicken-pox. Two months ago sore throat, enlargement of cervical glands, pale, no appetite, no pain, weak. One month, hard swelling in abdomen.

Examination. Pale; tonsils enlarged, mouth breather. Chest: soft bruit at apex of heart; superficial glands slightly enlarged, spleen and liver much enlarged; retinitis (right); urine negative. Never any hemorrhages; temperature elevated.

Blood. Erythrocytes, 2,700,000; leukocytes, 240,000 to 250,000; small lymphocytes, 7 to 13 per cent.; large lymphocytes, 32 to 56 per cent.; polynuclears, 16 to 22 per cent.; myelocytes, 12.1 to 27 per cent.; eosinophiles, 0.6 to 2.6 per cent.; eosinophilic myelocytes, 0.7 to 3.4 per cent.; mast-cells, 0.3 to 4.4 per cent.; normoblasts numerous. Regarded as intermediate between lymphatic and myelogenous leukæmia. Died at four and one-half months after onset.

Case XI. (McCaw.[12])—Infant, aged twenty months. Family and personal history good. Three weeks ago began to walk feebly and stagger, drowsy, and apathetic. Two weeks ago swelling of glands in neck, enlargement of abdomen.

Examination. Not pale, though hæmoglobin 38 per cent. Glands in neck, axillæ, and groin enlarged; spleen much enlarged; liver enlarged. Urine: albumin, oxalic acid crystals.

Blood. Leukocytes, 810,000; lymphocytes, 99.2 per cent.; later petechiæ and once blood in bowel movement. Spleen and glands diminished in size. Died about six weeks after onset.

Case XII. (Taylor.[13])—Boy, aged ten years. Six weeks ago pain in legs, thirsty, yawning, enlargement of parotid and submaxillary glands, of liver, and left kidney.

Blood. Leukocytes, 15,000; lymphocytes, 46 per cent. A few days later leukocytes, 50,000; lymphocytes, 94 per cent., with increase in size of glands. Hemorrhage from mucous membranes. Died twelve weeks after onset. Autopsy showed general lymphatic infiltration.

Case XIII. (Geissler and Japha.[14])—Boy, aged five years. Family history negative. Previous history, chicken-pox. Two months before became ill with fever, pain and swelling of abdomen, pain in feet, and later in all joints, general weakness; symptoms persistent ever since.

Examination. Well nourished, no rickets, chest negative, abdomen negative; urine negative; no swelling of joints nor pain on movement; no exanthem; slight enlargement of submaxillary and inguinal glands.

Blood. Hæmoglobin, 55 per cent.; erythrocytes, 2,200,000; leukocytes, 18,800; lymphocytes, 80 per cent. A few normoblasts, no poikilocytosis. Later petechiæ, nose-bleed, great enlargement of spleen and liver, no glandular swelling, increasing bone pains. Blood during the next three months ranged as follows: hæmoglobin, 22 to 60 per cent.; erythrocytes, 158,000 (after a nose-bleed) to 2,208,000; leukocytes, 12,000 to 34,150; polynuclears, 3 to 24 per cent.; mononuclears, 76 to 97 per cent. Poikilocytosis, many

megaloblasts temporarily after severe hemorrhages, many megalocytes in groups and about four times as large as a red corpuscle. A few neutrophilic and eosinophilic mastzellen, polychromatophilia. Death about five months after onset. Case at first might have been regarded as one of subacute rheumatism had it not been for the blood examination.

CASE XIV. (Glinski.[15])—Boy, aged one year. No family history. No previous history. For indefinite time pallor, malnutrition, vomiting and diarrhœa; prominence of eyes.

Examination. Pale, poorly nourished, submaxillary and cervical glands enlarged; bronchopneumonia on both sides; heart weak; spleen enlarged and hard; liver not enlarged; marked exophthalmus.

Blood. Hæmoglobin, 21 per cent.; erythrocytes, 918,750; leukocytes, 180,416; lymphocytes, 94.4 per cent.; neutrophiles, 5.3 per cent.; a few myelocytes and nucleated reds. Died with symptoms of pneumonia and heart failure. Autopsy, widespread leukæmic changes, especially in pia mater.

There can be no doubt of the diagnosis of leukæmia in any of the above cases. In all but Cases II., IV., and V. the blood count settles it beyond question. In Case II. there is no doubt of a marked leukocytosis, even though no total white count is given, the proportion of white to red being 1 to 12. The differential count was probably modified by the pneumonia, for we find 28.8 per cent. of polymorphonuclears, a high proportion for leukæmia. The total mononuclears, 60 per cent., would not be high for an eight months' infant in health, but is rather high for a leukæmia with 10 per cent. of myelocytes, and, together with this percentage of the last-named cell, justifies classing the case as one of the mixed-cell variety. Finally, the diagnosis is clinched by finding at autopsy typical leukæmic changes. As to Cases IV. and V., the advocates of von Jaksch's anæmia as a distinct disease might possibly class them as such; but I cannot recognize that anæmia as a distinct and separate disease, as a primary anæmia. It is secondary, the result of a variety of causes, chief among which are rachitis, syphilis, and severe intestinal disturbances. There is nothing in the reports of these cases to lead one to class them as secondary anæmia, while the leukocyte counts of 21,000 and 33,000, with the lymphocyte counts of 87 and 78 per cent. justify the diagnosis of lymphocytic leukæmia. That such comparatively low counts do occur in leukæmia is evidenced by Case XII. above, where were found at first a total count of 15,000, a lymphocyte count of 46 per cent., which figures a few days later had increased to 50,000 and 94 per cent., respectively.

My own case, now to be given in detail, also shows how low the total count may go. The history of this case, attended by Dr. John W. Fletcher, of Winnetka, and myself is as follows:

September 1, 1903. A. B., aged four years.

Family History. Maternal great-grandmother and paternal grand aunt died of phthisis. Father had trouble with ankle in infancy, said to be tubercular; outgrew it apparently, but for two or three years before birth of patient had more trouble with same ankle, though an exact diagnosis was never made. Two brothers, aged seven and nine years respectively, are well, but not robust, the former having adenoids. Sister, two months old, apparently healthy.

Previous History. Well at birth. Breast exclusively for three weeks; then breast and modified milk until seven or eight months, when weaned. General health has always been good, except that at times since early infancy the skin has shown marked pallor. An attack of acute tonsillitis in December, 1902. Has had none of the acute diseases of childhood. Appetite has been good, as a rule. Bowels generally regular, occasionally constipated.

Present Illness. For two or three months patient has had little appetite, and has shown a gradually increasing waxy pallor. There have been absolutely no other symptoms. The diet has been deficient in all directions, though more especially in the matter of fats and proteids. He has been up and about, out doors playing, has slept well, has not been fretful, bowels have been regular. In a word, except for his loss of appetite and great pallor, he has seemed perfectly well.

I first saw him professionally on September 1, 1903, at which time the result of the physical examination was as follows:

Physical Examination. Development and nourishment excellent, marked waxy pallor of skin and mucous membranes, shotty feel to cervical glands, both tonsils enlarged. Chest: area of cardiac dulness normal; apex, fourth space just inside mammillary line. Heart sounds strong and vigorous; soft systolic murmur heard generally over præcordia, but loudest at the apex; no bruit in neck. Pulse 96, regular, good strength. Lungs negative. Abdomen negative. No signs of hemorrhage anywhere; no tenderness over long bones. Blood: erythrocytes, 3,500,000; leukocytes, 10,000; hæmoglobin, 75 per cent. (Tallquist).

Directions were given to increase his diet in all directions, and he was given liquor potassi arsenitis in gradually increasing doses.

September 9th. Urine, 400 c.c.; specific gravity, 1021; no albumin, no sugar. Sediment: slight excess of leukocytes, a few renal cells, a very few normal blood corpuscles.

15th. Eats more under compulsion, but is no better; weight, forty pounds. Urine: specific gravity, 1020; no albumin, no sugar. No excess of indican. Sediment as before.

17th. Patient more easily tired, and is fretful. Physical examination: pallor is more marked, petechiæ present on neck, trunk, and limbs; not numerous; noticed by mother two days ago. Numerous black-and-blue spots in various places. No tenderness over the bones. Chest as before. Abdomen: spleen is felt one

inch by one inch below the ribs. Liver not enlarged, no distention. Blood (see table). Diagnosis: lymphatic leukæmia.

20th. Seen in consultation with Dr. Frank Billings, who concurred in the physical examination as reported above and in the diagnosis. Blood (see table).

21st. Ten c.c. of blood withdrawn from the median basilic vein by Dr. Ludwig Hektoen, who subsequently reported presence of the streptococcus.

22d. Sixty c.c. of human blood serum withdrawn yesterday from a vigorous woman were injected into the patient at 9.30 A.M. At the suggestion of Dr. Fletcher *x*-ray exposures were begun at 5.30 P.M. under the direction of Dr. W. A. Pusey. Blood (see table). Temperature, same.

23d. Much pain and discomfort from the serum injection. A few petechiæ. Blood (see table).

24th. Temperature higher, otherwise condition the same. Daily salt enema begun.

25th. Blood (see table).

26th. Spleen not felt and apparently not enlarged on percussion. Pulse between 132 and 134, strong and regular during the day, irregular during the night. Heart action strong and regular; murmur more intense and heard everywhere over cardiac area; some twitching of limbs; involuntary bowel movement at 8 P.M. Patient is decidedly worse. Blood (see table).

27th. Blood in bowel movements to-day for the first time; general condition same as yesterday.

28th. Much worse this morning; at times irrational and mildly delirious. More blood in bowel movements; pulse weaker, respiration becoming irregular. Oxygen started at noon—ten minutes, every twenty minutes.

29th. Moribund at 9 A.M. Unconscious and Cheyne-Stokes respiration at 10 A.M. Gradually sank, and died at 2 P.M.

Date.	Hæmoglobin.	Red.	Leukocytes.	Mononuclears.	Polymorphonuclears.	Eosinophiles.
September 1, 1903 . .	75 %	3,500,000	10,000	.....	.....	.....
" 16, " . . .	50 %	.....	Much increased.	99.5	0.5	.....
" 18, " . . .	45 %	3,116,000	30,000	98.9	1 0	0.1
" 20, " . . .	40 %	2,740,000	52,000	99.5	0.5	0.2
" 22, " . . .	40 %	1,892,000	80,020			
" 23, " . . .	.....	2,174,000	80,080	99.0	0.13	0.07
" 25, " . . . 5 P. M.	25 %	1,516,000	20.040			
" 26, " . . . 4.30 P. M.	20 %	1,544,000	6,300	98.2	1.55	0 3
				1000 cells 1 myelocyte?		1 normoblast.
" 28, " . . . 4 P. M.	15 %	1,280,000	8,000			

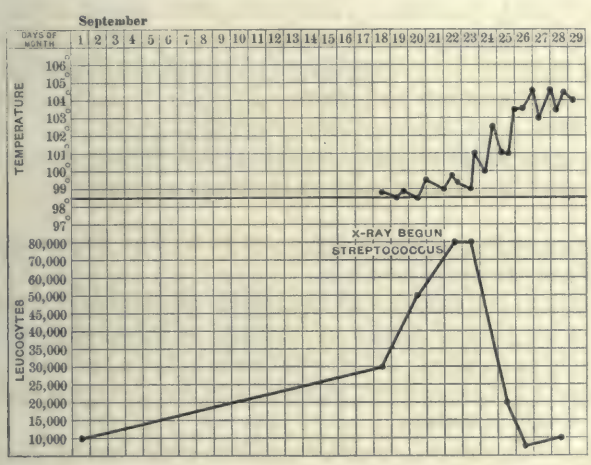
This case presents some points of extreme interest. First as to his heredity, the question of tuberculosis must be considered. The history of this trouble, three generations back, can have but little bearing on the case. The exact character of the trouble in the father's ankle apparently never was determined. On the whole, it is not probable that the tubercular taint played any part in the development of the child's final sickness.

When did this final trouble begin? This it is impossible to say. I saw the child frequently in a non-professional way throughout his life, and at times noticed his great pallor. Generally, however, he seemed perfectly well, so I said nothing to the family about his off days. His parents regarded him as the most robust one of three children. During the early part of last summer I noticed the increasing pallor, which was so great in early September that I then examined the child, with the result already detailed. There is no doubt in my mind that the malady began as early as last June or July, if not before. It is not at all improbable that the periods of intense pallor first noticed in infancy were in reality the beginning of his trouble. This, however, is pure speculation.

The absence on September 1st of all physical signs except the waxy pallor, enlarged tonsils, and condition of the blood is striking. The absence of hemorrhages until late in the disease is also quite remarkable. The presence of a few normal red blood corpuscles in the urine in the first examination may of course be regarded as a hemorrhage due to the leukæmic condition. The corpuscles, however, were very few in number, not more than one often sees in the urine of less serious conditions. There never was any nose-bleed, never any bleeding from the gums, and not until September 15th, two weeks before death, were any hemorrhages noticed under the skin. Indeed, the general absence of symptoms, except the pallor, were frequently commented upon by the parents. It was not until the onset of the acute symptoms with rapidly rising temperature, about six or seven days before death, that the child seemed acutely ill. It is unfortunate that I have not a record of his temperature during the first two weeks of September, but as he was up and out doors running around, the temperature was not taken. The three days' normal temperature, when systematic readings were first instituted, makes it probable that up to that time the temperature had been normal. I can but believe that the last week of illness simply marked the final acute stage of a chronic process which began months, possibly two or three years, before.

The chief interest of the case, of course, centres in the condition of the blood, especially in the leukocytes. The course of the erythrocytes, as a whole, shows a steady downward trend throughout the period of observation. That of the leukocytes is most interesting. (See chart.) Beginning with a normal count at the first examination, it rises rapidly during the first two weeks to 30,000, then still

more rapidly, reaching its maximum (80,000) five days later, when after two days more we see an ante-mortem drop to a point even subnormal—6300. The leukæmic agent, whatever it is, apparently was in the ascendancy during the first three weeks, and as a result of its action upon the bone-marrow a rapidly increasing leukocytosis takes place. Then, under influences indefinite and unknown, the upward march is checked, and is followed by a rapid descent. It is possible that the fall in this case was due to the presence of streptococci found in the blood on September 21st. The organism, of course, may have been present before this date. This was our first bacteriological examination of the blood. The next day the leukocyte count reached its maximum, and the day after that began to drop. At about this time also the temperature began to rise rapidly. It looks as though these two phenomena, rapidly rising temperature and rapidly falling leukocytes, might be due to the invasion



by the streptococcus. The leukæmic agent, however, is still active, the lymphocytes registering 98.2 per cent. and the polymorphonuclears 1.5 per cent. in a total white count of 6300. What the differential count at the first examination was I do not know, as unfortunately I did not examine any dry cover-slips, the total white count being practically normal. The next examination, however, two weeks later, showed the great increase, 99 per cent., in the mononuclear elements, which characterized the blood condition up to the time of death, and this condition may have been present on September 1st. It simply shows that in these severe cases of anæmia we must not be content with a total white count alone, but must study our dry specimens.

Study of the dried smears prepared with the Wright stain shows interesting blood pictures. The mononuclear cells resemble in structure lymphocytes having a round or slightly indented nucleus

that nearly fills the cell and takes a deep stain. A remarkable number of basophilic granulations are seen. There is great variation in the size of these mononuclears, the diameter ranging from six to thirteen microns, yet the small variety prevails. It is probable that both large and small cells have a common origin, and that the various sizes and shapes are due to violence in manipulation, for the size and appearance of the cells vary in different parts of the same specimen, those in areas where the layer of blood is thick, and where, therefore, they are protected from pressure in the process of spreading, being small and deeply stained; whereas, in areas where the smears are thin, and where, therefore, pressure is greatest, they are larger and less deeply stained, suggesting spherical lymphocytes that have been flattened out. Again, the edges of the larger forms are often uneven and ragged; the cell protoplasm is usually undemonstrable, as if the ectosarc had ruptured, leaving only the round nucleus. That such great changes were brought about by the process of smearing is attributable to the extreme friability of the cells. According to Capps* this friability and consequent cell variation are greater in acute leukæmia than in the chronic form.

Red corpuscles show considerable poikilocytosis, increasing with the course of the disease. Nucleated reds are rare.

Following is the report of the autopsy by Dr. Bassoe, pathologist at the Presbyterian Hospital:

Anatomical Diagnosis. Hyperplasia of intra-abdominal lymph glands, spleen, and intestinal lymph follicles; general anæmia; multiple hemorrhages of serous membranes, kidneys, myocardium, and bone-marrow; accessory spleen; agonal intussusceptions of small intestine.

The body is that of a well-nourished child, rather large for his age. The skin is very white. The external lymph glands are not enlarged. The peritoneal cavity is empty and free from adhesions. The pleural cavities are both empty, and there are no adhesions. The pericardial cavity contains a few cm. of clear fluid. The thymus is about 4½ cm. long by 2 cm. wide and 1 cm. thick. The tissue is very pale. Each lateral lobe of the thyroid measures 2½ x 1½ cm.; on section it is pale, grayish-red, and glistening. The mucous membrane of the larynx and trachea is smooth and extremely pale. The tracheal and bronchial glands are moderately enlarged, the largest being 18 x 10 x 3 mm., dark red externally and on section.

The weight of the left lung is 105 grams. The pleura is mottled, light gray and red, with small ecchymoses here and there. It crepitates throughout. The section is very pale and grayish-white. The

* Oral communication.

weight of the right lung is 125 grams, and is in the same condition as the left.

In the heart the epicardium is covered with a large number of ecchymoses. The tricuspid admits three finger-tips, the mitral admits one readily. The valve shows no changes. There are a few ecchymoses in the epicardium of both ventricles and the right auricle. The foramen ovale is closed, the myocardium is light-gray brown generally, but dark-red areas are seen throughout the entire thickness of the ventricular walls. The weight is 100 grams.

The spleen is smooth and weighs 90 grams. It measures 11 x 6 x 3½ cm. On section it is dark red, mottled with whitish bands and dots. At hilum an accessory spleen 1 cm. in diameter. The aorta is smooth. The pharynx was not examined. The œsophagus is smooth. The membrane of the stomach is smooth, with numerous reddish areas which do not disappear readily on pressure.

In the small intestine there are six descending agonal intussusceptions. The mucous membrane of the duodenum is pale and bile-stained, with solitary follicles enlarged. Peyer's patches are of a dark-grayish color and prominent, at about the ileocæcal valve is a patch 5 cm. long occupying the entire circumference. The appendix is 8 cm. long, and the lining is smooth. The solitary follicles are prominent throughout. In the sigmoid are a few blood-stained crusts.

The liver is 565 grams in weight, and smooth externally. On section it is a light grayish-brown in color, and but little blood exudes on pressure. The lobular markings are invisible, and the cut surface is of a homogeneous appearance. The gall-bladder contains fluid bile and the lining is smooth. The pancreas is of normal size and extremely pale. The adrenals are small and pale. The kidneys weigh 130 grams. The left measures 8½ x 5 x 3 cm. The capsule is not adherent and leaves a pale-gray surface, on which are a large number of ecchymoses, the largest measuring 6 mm. in diameter. On section it is extremely pale, the pyramids are white entirely, and the cortex markings can be made out in places. The section also has an area of small ecchymoses. There is a narrow reddish line between the pyramids and the cortex. The capsule is thin. The right kidney is the same size and contains a small amount of yellow fat. Otherwise it is the same as the left. The ureters are small. The bladder is extremely pale.

Lymph Glands. The retroperitoneal glands are moderately enlarged, the largest being 12 mm. in length and very dark. On section it is mottled grayish-red, and in places almost black. Those about the pancreas are the largest, the periaortic glands are of similar appearance. The mesenteric glands are uniformly prominent and dark red in color, but smaller. Cervical, axillary, and inguinal glands are not enlarged, but the iliac glands are slightly so.

The marrow of the sternum is of the usual deep-red color. The

marrow of the femur is also very red, with darker hemorrhagic foci.

The brain was not examined.

The meninges of the cord are very pale. The cord is preserved intact.

Microscopic. Heart Muscle. The section shows in several places infiltrating hemorrhage into the myocardium. The muscle fibres are forced wide apart by the blood. The number of leukocytes does not seem to exceed much the normal. A large per cent. are of the small mononuclear variety, with deeply staining nuclei. In parts of the section containing no hemorrhage the muscle appears normal.

Right Lung. In the upper lobe areas are found in which the alveoli are filled with a granular material containing many leukocytes. Between these areas there are areas showing compensatory emphysema. In the first-mentioned areas the walls of the alveoli are somewhat thickened, but not greatly congested. There is a noticeable increase in the nuclei in the walls. The leukocytes within the alveoli vary in kind. There are small mononuclear and polymorphonuclear and large mononuclear and polynuclear epithelioid cells, some of which contain pigment granules, also some cells which look like plasma cells. The epithelium of the bronchi is not in good condition, but it is in most cases found broken up within the lumina.

Left Lung. Lower lobe presents similar changes.

Liver. The liver cells are small and vacuolated, as if they were the seat of fatty degeneration. The spaces between the cords of cells are filled with a granular material. The interlobular vessels are surrounded by connective tissue, which is infiltrated with cells. The intralobular veins appear small. In the one large vein are many cells which have the same appearance as the surrounding liver cells. In one place a small lobule, surrounded by abundant connective tissue, gives the appearance of a cirrhotic liver.

Kidney. The vessels contain but little blood. The glomeruli show some increase in the number of nuclei, and there are some with ragged outline, and masses of cells with granular material in Bowman's capsule. The capsule is not thickened.

Convoluted Tubules. The cells are indistinct in outline, and here and there is found a cell within the tubule. The lumen is filled with granular material. The outlines of the straight tubule are in many cases made up of the basement membrane, with epithelial cells scattered within the lumen. Other tubules appear normal. The connective tissue shows no increase, but in many places is packed with leukocytes.

Pancreas. The pancreas shows very marked necrotic changes, which seem post-mortem in origin.

Spleen. The spleen presents in the section a mottled appearance, due to areas infiltrated with blood, alternating with areas contain-

ing little blood. This makes the Malpighian corpuscles for the most part hard to distinguish. The mottled appearance of the section gives it somewhat the appearance of a section of hæmolymph gland. In the hemorrhagic areas it is difficult to tell whether the nucleated areas seen are the pulp cells or leukocytes brought by the blood. The stroma is not to be seen in these areas. There are a few polymorphonuclear leukocytes.

Thyroid. The thyroid contains a moderate amount of colloid, occurring in masses separated from the walls of the acini by a large space. The epithelium is found desquamated in most of the acini and lying in the space surrounding the colloid. In many cases the acinus is entirely filled with small epithelioid cells, and there is an extensive cell infiltration throughout. On one edge of the section is a large quantity of pigment, probably the remains of hemorrhage. The suprarenal shows little change. The stomach contains areas of hemorrhage in the superficial layer of the mucosa, otherwise it appears normal.

Small Intestine. The mucous membrane is necrotic, and throughout nearly the whole length of the section, which is longitudinal, the submucosa is infiltrated with lymphoid cells. Near the muscularis these cells are somewhat far apart. Nearer the lumen they are densely packed, and at the surface they have undergone necrosis, and, with the remains of the mucous membrane, form the lining of the lumen.

Section through a Peyer's Patch. The mucosa shows the same change as in the other section. The centre of the individual follicles of the patch contain lymphoid cells, widely separated by granular material containing elongated irregular nuclei. The surrounding lymphoid cells are more densely packed, then become more loosely distributed for some distance in the submucosa. Near the lumen they show necrotic changes, as described in the other section.

Thymus. The organ is large, and the section shows remarkably little change from the infantile type. The corpuscles of Hassal are large, with blue-staining (hæmatoxylin) centres in many cases. It is lobulated, in the infantile form, but the lobules show no differentiation into cortex and medulla. The lobules are well filled with lymphadenoid cells. Many cells similar to these are found in the connective-tissue septa, and a few in the corpuscles of Hassal.

Accessory Spleen. The section shows the characteristic splenic capsule, with trabeculæ penetrating the gland. The parenchyma has the same structure as described in connection with the spleen.

Lymph Gland. The arrangement into lymph cords and channels is not very plainly marked, the lymph cords being so thin and containing relatively few lymphadenoid cells. Around the periphery of the gland the lymphadenoid cells are more abundant. The lymph channels contain many cells of the endothelioid type. These

are almost as numerous as the large and small lymphocytes. The number of cells in the channels is not more than normal.

Hæmolymph Glands (Retroperitoneal). Here the well-filled cords of lymph cells stand out in marked contrast to the blood-filled sinuses. The gland is of the splenic type. The circular sinus is very well made out in most of the periphery. Contrary to the usual finding, the central blood sinuses are packed with blood. This blood contains very many small mononuclear leukocytes, and also large mononuclear leukocytes. A few of what appear to be nucleated red cells are present, but there is no certainty of the identity of these, as there are many lymphocytes containing a minimum amount of cytoplasm surrounded by red cells. No hæmolysins could be made out with certainty, but very pale outlines of corpuscles with granular masses surrounding them, the granules staining as hæmoglobin, indicate some hæmolysis. There is little phagocytosis. In another gland the destruction of red cells is more plainly indicated. The spinal cord was negative; cultures therefrom were sterile.

Bone-marrow. The bone-marrow from the shaft of the femur and that from the sternum, in contrast to the normal, appear very similar. The marrow of the shaft of the femur shows little of the normal narrow reticulum surrounding fat vacuoles. Most of the vacuoles are absent, and the space is all occupied by a reticulum filled with blood containing large numbers of nucleated red cells(?). There are but few giant cells present. In most places the red cells are disintegrated into a granular material. There appear to be some nucleated red cells present, but, as in the hæmolymph glands, these cannot be made out with certainty.

The marrow from the sternum presents a similar appearance, but there are not so many red cells present, and the structure is more plainly made out. There are a few myelocytes present.

Bouillon emulsions were made from the lung, liver, spleen, and bone-marrow, and from these glycerin-agar slants were inoculated. No results after seventy-two hours. From the heart's blood the streptococcus was obtained in pure culture. The bile was sterile.

Study of this excellent report of Drs. Bassoe and Dick shows only what has been observed in previous cases. There are noted in organs and tissues generally the infiltration with lymph-adenoid cells, closely resembling the small mononuclear lymphocytes seen in the blood during life, showing the widespread distribution of these elements. The involvement of the bone-marrow is confirmatory of the views of Neumann and others, that no case of leukæmia thoroughly studied has failed to show an abnormal condition of this structure. Cultures from the bone-marrow, however, were negative. The presence of streptococci in the blood both during life and post-mortem observed in this case has also

been noted in other instances. The enlargement of the thymus noted here has also been observed by Rocaz. It is to be regretted that through an oversight no animal inoculations were made.

Morse's report of 8 cases, McCrae's of 6, and my own of 15 now give us 29 cases of acute leukæmia for study. It must be confessed, however, that their analysis adds little to our knowledge of the condition. There seems to be nothing in family or previous history which can be regarded as predisposing to the disease. The family history of tuberculosis in my own case led me to look up this point in others, Unfortunately such history is given in comparatively few instances. In 105 cases 51 make no mention of family history at all, and of the remaining 54 cases 41 are negative, and 14, or 26 per cent., have a family history of tuberculosis. Susmann,[16] studying the relation of leukæmia and tuberculosis, even concludes that a certain antagonism exists between the two conditions. The leukæmic condition improves, the total leukocyte count diminishing, the neutrophiles increasing. Following this hint injections of tuberculin have been tried in a few cases, but nothing conclusive has been determined thereby. It is not probable from the data available that tuberculosis plays a part either direct or indirect in the cause of the condition.

As to direct heredity, there have been reported only two cases of the condition in parent and child, too few from which to draw any conclusions.

As with heredity, so with the previous history of cases, nothing appears to act as a predisposing cause, except, possibly, chronic tonsillitis. A large proportion of cases show this condition, but here the question arises whether the tonsillar condition is not the result rather than the cause of the process. It is not improbable, however, that the infectious agents found in the late stages of leukæmia gain access to the system *via* the tonsils, and that to this extent at least the diseased condition of the latter may contribute to the final outcome.

No age is exempt. Leukæmia has been observed in the newborn child, and as late in life as seventy-one years.

The onset may be sudden, but more often is insidious, with vague indefinite symptoms, which gradually develop into the typical leukæmic picture.

The general course of the disease in children, on the whole, is the same as in adults, and is always fatal. It occurs more frequently in males, 21 of the 29 cases being boys. The spleen was enlarged in all cases, the liver generally, though the enlargement of neither was great. A not infrequent phenomenon was a diminution in the size of the spleen before death. General glandular enlargement was by no means constant, the cervical glands being most frequently involved.

The duration of the cases was from four and a half days to five

months. Six, possibly seven, of the cases were prolonged beyond the conventional nine weeks. The onset, however, is usually so insidious that it is impossible to determine exactly when a case does begin. Hence the impossibility of drawing a hard-and-fast line—*e.g.*, at nine weeks as the limit for acute cases. The acute part of the disease is undoubtedly but the final stage of a chronic process, the exact beginning of which we cannot determine.

Nor does the duration depend upon the type of the disease. The most prolonged case, five months, was lymphocytic, whereas the one myelocytic case lasted about two and a half months; and of the two mixed cases one died at the end of four and a half months, the duration of the other was unknown, but was probably short. (Case II.)

As in the adult, the chief interest in leukæmia centres in the blood. There is, of course, the diminution in erythrocytes and hæmoglobin. The lowest red count recorded is 750,000, and this was after severe hemorrhages. The leukocyte counts ranged from 6000 to 810,000. Several low counts have been observed, and always just before death. A falling white count, as in my own case, is apparently indicative of approaching death. Age apparently has no effect upon the total white count; thus of two thirteen-months-old children one had a count of 21,000, and the other 208,000, and the highest count, 810,000, occurred in a twenty-months-old infant.

The differential count showed that of the 29 cases 25 were of the lymphocytic type, 1 myelocytic (Case VII.), 2 of the mixed-cell variety (Cases II. and X.), and 1 case undetermined. The preponderance of the lymphocytic type is thus emphasized anew. The lymphocytosis, furthermore, is more apt to be of the small variety; this cell predominated in 12 cases, the large cell in 3, the two varieties equal in 2, and in the other cases no attempt is made to distinguish between them. The degree to which the lymphocytosis may rise is shown in my own case, where were found constantly 99 and 99½ per cent. of lymphocytes. The degenerated granular character which these cells may undergo is also well illustrated in the same case.

The polymorphonuclears are always reduced, often to an extreme degree. Thus in one specimen from my own case I counted 1100 cells before finding a neutrophile; in the same specimen also but one eosinophile was seen. The total count here being 80,080, the absolute number of each variety in a cubic millimetre of blood was as follows:

Mononuclears[1]	79,919.8
Polynuclears	80.1
Eosinophiles	80.1
	80,080.0

Whatever the function performed by the neutrophiles, obviously it could not be carried on properly by such a small number of cells.

Except in the myelocytic and mixed cases, myelocytes were rarely present, and then only in small numbers. Nucleated reds were also rare, though found occasionally, especially in young subjects; thus case IV., thirteen months old, showed eight normoblasts and eight megaloblasts in a count of 200 cells, a striking example of the tendency of the blood in infancy to revert to the fetal type under pathological conditions.

Certain minor differences in the behavior of the disease in early life are observed. Thus, in children hemorrhages are apparently less frequent and less severe; in the 29 cases hemorrhage occurred in only 17, and in only 1 of these was it severe. It occurs in the nose, mouth, bowels, kidneys, and skin. The blood picture also represents a greater variety than in adults, and the lymphocytosis is more apt to be of the small type.

In an explanation of the abnormal blood picture, of this turning upside down of the different varieties of leukocytes, lies the solution of the whole leukæmic problem. The change is undoubtedly the result of a chemotactic agent acting upon the bone-marrow, the clinical manifestations and type of disease depending upon the nature of this chemotactic agent whatever it may be. Of the real nature of this agent and of its action upon the bone-marrow we know nothing.

The diagnosis of leukæmia can be made only by a complete examination of the blood. Profound anæmia and leukocytosis are so frequent and arise from such a variety of causes in infancy and childhood, that there is more chance of error in early life unless one makes a differential white count, the only means by which a diagnosis can be clinched. In the absence of marked symptoms a constant and comparatively high lymphocytic count (90 per cent.) must be observed, owing to the great ease with which a lymphocytosis is set up at this time. Thus I was somewhat disturbed once at finding in a pale twenty-two-months-old infant with hypertrophied tonsils, adenoids, and enlarged cervical glands, a white count of 20,000 and 70 per cent. of lymphocytes. Subsequent examinations, however, showed a normal condition of the blood. Conversely a leukæmia with marked throat symptoms may be mistaken for an ordinary acute infection. There is little danger of confusing leukæmia with pertussis.

The effect of intercurrent disease or infection upon leukæmia is interesting. This subject has been carefully studied by Dock[17] and others, and in a general way it may be said that there is almost always a fall in the total leukocytes, and also, though less uniformly, there is a disposition for the leukæmic character of the blood to disappear more or less completely and for the polynuclear to in-

crease absolutely as well as relatively. The total leukocytes have been known to fall as low as 471. Case II. in my own series, for example, shows the effect of a double pneumonia in an eight-months-old boy; we find 28 per cent. of polynuclears and 65 per cent. of total mononuclears. The influence of tuberculosis has already been mentioned. Dock's study shows the effect of influenza, erysipelas, acute and chronic tuberculosis, abscess, etc.

Turning now to the pathological side of the question, the results of autopsies do not throw much light on the problem. Post-mortem examinations in adults and children have shown the widespread distribution of the disease, abnormal appearances having been found in practically all organs and tissues of the body. The condition found most commonly has been an excessive infiltration of tissues with small mononuclear lymphoid cells, identical in appearance with the smaller lymphocytes with which the circulating blood is flooded during life.

Perhaps the most important contributions which have been made to the pathology of the subject are those which have shown that the bone-marrow *only* need be involved in order to produce the disease, whether of the myelocytic or lymphocytic type. For the researches of Neumann, Walz, Pappenheim, Brandenberg,[18] Kelly,[19] Reed[20] and others have shown that the bone-marrow is *always* involved, the glandular system sometimes not at all, sometimes only slightly, as in my own case; and they maintain that no case which has been thoroughly studied has failed to show a pathological condition of the bone-marrow. The incorrectness of the terms "lymphatic" and "myelogenous" is thus obvious. All cases are "myelogenous"—*i. e.*, of bone-marrow origin. The terms "myelocytic" and lymphocytic," suggested by Kelly and others, are preferable for the present, even though they are based on a physical sign, *i. e.*, on the presence of either myelocytes or an excess of lymphocytes in the circulating blood.

The description of the bone-marrow given in my own case is typical of the changes found in this tissue. These changes are not always found in all parts of the bone-marrow. They may be localized, and are found most commonly in the shafts of the long bones.

The comparatively few bacteriological investigations which have been made are of a negative value. Streptococci and staphylococci have been found in the blood during life, also these and other familiar organisms have been found in the blood and tissues post-mortem, but no specific organism which can be considered as causing the condition. It is probable, furthermore, that these organisms are secondary invaders. Nichols[21] found in 92 cases showing bacteria that in chronic leukæmia organisms were found oftener in the terminal than in the earlier stages. They are probably the result rather than the cause of the original underlying processes, and, as already mentioned, the frequent occurrence of

hypertrophied tonsils in leukæmic cases suggest that they may have gained access to the system by this route.

Thus, lacking knowledge as to the exact cause of leukæmia, various theories have naturally been advanced to explain the disease. Nichols[21] has studied these various theories, grouping them under three heads: (*a*) toxic, (*b*) infectious, and (*c*) cancerous or hyperplastic. Of these only the infectious theory has been studied experimentally, and the results here have been negative. Discussing the cancerous theory, he likens the enormous number of leukocytes in leukæmia to the proliferation of epithelial and connective-tissue cells seen in carcinoma. He finally concludes that until the true nature of leukæmia is understood both the toxic and cancerous theories must be considered among the possible causes of the disease.

Nichols' paper is exhaustive and valuable, but study of it and leukæmic literature generally suggests the desirability of further investigations in two directions: injections of blood from living leukæmic patients directly into the bone-marrow of animals, and, secondly, injections of pure cultures of various pathogenic organisms into the same structure. As far as I have been able to learn from a pretty careful review of the literature, such investigations have not been carried out with pathogenic organisms at all, with leukæmic blood but once, and then with a negative result. Accepting as we must the bone-marrow as the primary pathological lesion of the condition, our efforts should be directed toward ascertaining the nature of the agent producing that marrow change. Fascinating and absorbing as is the study of leukæmic blood, the condition found there represents, after all, only one physical sign of the disease. The real question is, *why* do the bone-marrow and the other blood-making organs produce this kind of blood, *what* is the agent causing the organs to manufacture 99 per cent. of lymphocytes instead of 40 per cent., or to set free in the circulation 27 per cent. of myelocytes instead of an occasional one?

Treatment is of no avail. Arsenic is generally given, but is useless. The record of cases treated with the *x*-ray thus far gives no promise of permanent help. The hope that such treatment may be of service is based presumably on the theory that leukæmia is a malignant disease of the bone-marrow. Granting the truth of this there is less chance of the improvement seen in more superficial malignant disease, owing to the fact that calcium salts offer greater resistance to the passage of *x*-rays than do other constituents of the body; hence the greater difficulty of affecting bone-marrow.

The natural behavior of leukæmia in patients attacked with an intercurrent disease, suggests a method of treatment not hitherto tried to any extent. If the fall in total leukocytes, the attempt to resume a normal leukocyte formula, and the reduction in splenic enlargement, phenomena already mentioned, in reality be due

to the newly invading agent, it seems not unreasonable to hope that injections of sera, anti-streptococcic, anti-pneumococcic, etc., might accomplish the same result, and thus bring about an amelioration of the most prominent pathological conditions of the disease. True, no case thus complicated has ever recovered, nor has tuberculin been of permanent value; still in a disease as obscure and as uniformly fatal as is leukæmia, any methods of treatment are justifiable. Sera injections seem worthy of trial.

CONCLUSIONS. All cases of leukæmia are myelogenous in origin. As in adults, the acute variety is more apt to be of the lymphocytic type.

The disease is rare in early as well as in later life. It is probably more common than has been supposed, however, 22 cases of the acute or subacute variety having been reported since 1898, while previous to that date only 7 cases are on record.

The course in children differs from the adult type only in minor details; hemorrhages are fewer and less severe, the lymphocytosis is more apt to be of the small variety. The disease is always fatal.

It is suggested to use injections of sera in treatment.

Experimental inoculations with leukæmic blood and with cultures of pathogenic organisms are desirable, such inoculations to be directly into the bone-marrow.

I am much indebted to Professor Hektoen, Drs. Bassoe and Dick for the thorough pathological report, and to Dr. Joseph A. Capps for valuable help in the examination of the blood.

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A CASE OF ACUTE LYMPHATIC LEUKÆMIA.

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At the beginning of the nineteenth century pallor of the blood, as if mixed with pus, was observed by Bichat. This appearance combined with enlargement of the spleen was observed by Velpeau[1] in 1827. The alteration in the blood depending on an excess of leukocytes Donne described and interpreted in 1844 as due to imperfect transformation of white into red blood cells.

In October, 1845, Hughes Bennett and Dr. Craigie[2] published two cases of the disease, and to the former appears to belong the credit of recognizing the salient features of the affection as a distinct malady. In November, 1845, Virchow[3] published another case independently and admirably worked out.

In all these cases the change in the blood was only recognized after death. Virchow proposed the name leukæmia and Bennett leukocythemia. It was first observed during life by Dr. H. M. Fuller in 1846 and subsequently by Dr. Walshe.

In 1848 the first case during life was diagnosed by Vogel. Ebstein,[4] in reporting several cases, calls attention to the fact that traumatism may play an important role in the etiology. A. Fraenkel,[5] in organs from a case of leukæmia, pointed out that there was present a lymphoid infiltration, especially of the kidney. Herman Suchannek[6] found in the nasal mucous membrane that the olfactory epithelium was normal, but that the glandular structure was destroyed by the infiltration of lymphocytes. Monro[7] cites a case of leukæmia in which there were found on histological examination numerous small oval bodies in the heart, between the fibres, smaller than nuclei of leukocytes, and too irregular in size to be regarded as bacteria. They were not present in any other organ. Grewe[8] reports a case of acute lymphatic leukæmia following a strain in lifting a weight, in which the blood was characteristic of lymphatic leukæmia. At autopsy, the lymph glands were enlarged, spleen hypertrophied, and the liver and kidneys contained lymphoid nodules. Palma[9] reports a case of primary sarcoma of the thymus with secondary deposits in the lymph glands. A month later the patient showed an increase in the number of leukocytes and Palma concluded it to be a case of lymphatic leukæmia preceded by pseudo-leukæmia. Dock[10] mentions a case of chloroma, which condition

was most marked in the periosteum in and about the orbit, and numerous widespread metastatic nodules, all of a pea-green color. The polynuclear leukocytes averaged 20 per cent., the small lymphocytes 7 per cent., and the large lymphocytes 65 per cent. Normoblasts occurred in the proportion of two to five per thousand of red corpuscles. Only one eosinophile could be found "out of many thousand leukocytes counted."

Fraenkel believed that the large lymphocytes could be regarded as pathognomonic of acute lymphatic leukæmia. Hirschloff reported two cases of leukæmia in which most of the leukocytes were large mononuclear cells without granules; some, however, contained neutrophilic and some eosinophilic granules. According to Birch-Hirschfeld and Benda the variation in size may have an anatomical basis in the hyperplastic lymph nodes, as in some cases these contain mostly small lymphocytes. Müller claims that myelocytes (both neutrophilic and eosinophilic) and mast-cells are usually absent or extremely scarce in leukæmia. Polynuclear leukocytes (both neutrophilic and eosinophilic) are also comparatively scarce. Nucleated reds are usually very scanty and may not be found at all, according to Ewing.[11] Intercurrent affections may greatly alter the appearance of the blood in leukæmia. Fraenkel cites a case in which the leukocytes fell from 220,000 to 1200, and ascribes it to a pure leukocytolysis. After typhoid fever, pneumonia, empyema, erysipelas, septicæmia, tuberculosis, and carcinoma the same changes have been noted.

Kraus recently reported a case in which the leukocytes fell from 393,000 to 4000 as the result of double pneumonia and empyema. The viscera showed no evidence of leukæmic infiltration and he inferred that the infection had not only transformed the blood, but had resolved the essential visceral lesions as well.

After the subsidence of the infection, the blood soon resumes its original condition, according to Grawitz. The reduction of leukocytes can also be accomplished by experiment, as in a case cited by Jacob, which showed 850,000 reduced to 282,000 by the injection of glycerin extract of spleen. Richter obtained the same results by injecting spermin; and Henck[12] by injection of tuberculin. Kinnicutt[13] reports a large number of eosinophiles in the blood in a case of leukæmia. Nobl[14] regards the mitoses of Müller as the only certain evidence of leukæmia. In two cases examined the eosinophiles were scanty. In Uthemann's[15] case 93 per cent. of the white cells were lymphocytes. According to Osler[16] eosinophiles and nucleated red corpuscles are rare and myelocytes are not present. Cafafy[17] claims that the amœboid movement of the white cells is feeble, due in all probability to the large number of mononuclear elements present. Of 16 cases of leukæmia reported by A. E. Taylor,[18] 12 presented an increase in the number and percentage of mast-cells. In the remaining 4 cases no mast-cells were demon-

strable. He stated that not one of the cases showed 4,000,000 red cells, and claimed that there was always an oligocythæmia present. He considers the condition to be due either to cachectic or nutritional disturbances, to toxic hemolysis, or to disturbances in the bone-marrow. Polychromatophilia and poikilocytosis are almost constant features in leukæmia. Nucleated red cells, most of which were normoblasts, were found in all but one case of the sixteen examined. Microblasts, macroblasts, and poikiloblasts were also present. The lymphocytes were devoid of movement, while the myelocytes showed constantly slight motility. As low a percentage as 15.6 of polymorphonuclear leukocytes was noticed in one case. Eosinophilia was not constantly present in lymphatic leukæmia, while it was invariably present in myelogenous leukæmia. Leukoblasts, according to Löwit, can be found in developmental areas in the lymph glands, spleen, intestines and bone-marrow in acute leukæmia. In but one case of lymphatic leukæmia were circulating mast-cells demonstrable. Fraenkel admits that myelocytes may occur in acute lymphatic leukæmia, and Benda claims they are frequently, if not constantly, found in the circulating blood and that local basophilia is very common in leukæmia.

Dunn[19] cites leukæmia in a child of eight years, in which there was a crescentic tumor in each upper eyelid. The first evidence of the disease was a swelling in the parotid gland, which increased greatly in size and became as hard as stone.

Middleton[20] contributes 2 cases of leukæmia, one a child of sixteen months, the other a boy four years old. In the first the proportion of leukocytes to erythrocytes was 1 to 9. Paris[21] cites a case of leukæmia in a boy of seventeen years which after six days terminated fatally. Post-mortem examination showed the typical lesions of leukæmia in the spleen and liver, but the lymphatic glands were wholly normal. Eichhorst[22] also mentions acute leukæmia in a lad of eight years; the duration of the disease, fourteen days.

Vesemeyer[23] reports 3 cases of acute leukæmia terminating in three, five, and ten days, respectively; Ortner,[24] a child eight and a half months old, and Ebstein[25] reports a case ending fatally six weeks after the patient first came under observation. Ord and Copeman[26] call attention to a case of five years' standing; Lannois[27] one of three years' duration.

Saenger[28] records the occurrence of lymphatic leukæmia in a pregnant woman in which premature labor had to be induced on account of unbearable distention from uterus and spleen. He also calls attention to a case of congenital leukæmia, the child being stillborn in the thirty-second week. The blood upon examination showed one white to three red blood cells. The mother's blood was not examined. Litten[29] reports acute lymphatic leukæmia following influenza that terminated in three days; Guttman, a

child of ten years, in which the ratio of white to red cells was 1 to 1¼, and that only a single eosinophile was observed in a preparation; Wertheim, in a case of lymphatic leukæmia, found no nucleated reds, the white corpuscles numbering 480,000. Thayer[30] mentions that nucleated red cells are rare, and if present are likely to be megaloblasts. Müller found very few eosinophiles in a case of lymphæmia; Thayer[31] found 0.1 per cent.

Wilkinson[32] reported a case of leukæmia which, upon first examination of the blood, showed 560,000 leukocytes, chiefly myelocytes. Eight days later a second examination was made, when it presented all the features of lymphatic leukæmia, while only an occasional myelocyte was observed. Nucleated red cells—normoblasts and megaloblasts—were present, the latter predominating. At the first examination of the blood so much polymorphism of the white cells existed that an accurate differential count could not be made. No necropsy was obtained.

Nichols[33] reports 2 cases of acute lymphatic leukæmia. In one the leukocytes numbered 67,800 per c.mm., "all of which excepting a small proportion were large lymphocytes." A second examination made three days later showed 134,800 leukocytes per c.mm., in which the large lymphocytes numbered 91.3 per cent. and small lymphocytes 7 per cent. In this case a coccus was present "differing from the ordinary known cocci" in the blood and organs, but produced no specific action when inoculated into guinea-pigs and rabbits. In another case the leukocytes numbered 529,000 per c.mm. Eighty-five per cent. of them were large lymphocytes, 10 per cent. small lymphocytes.

A. O. J. Kelly[34] cited 4 cases of acute lymphatic leukæmia. The first showed 17,000 to 30,000 leukocytes, 93 per cent. of which were lymphocytes; the second (a young woman who had been delivered of a child a short time before), where the leukocytes ranged from 200,000 to 400,000 and the lymphocytes constituting 98 per cent.; the third, a young man in whom sepsis was suspected, a differential count of the blood showed 98 per cent. lymphocytes; the fourth, a man whose spleen was enlarged, where the leukocytes varied from 12,000 to 38,000.

Kelly doubts the non-identity of the two varieties of leukæmia—myelogenous and lymphatic. He bases his doubts upon several conclusions: 1. The occurrence of cases of so-called acute lymphatic leukæmia, with little or no enlargement of the lymph glands. 2. The demonstration of the predominance of lymphadenoid changes in the bone-marrow in every case of lymphatic leukæmia in which the bone-marrow has been examined—observed by Neumann many years ago. 3. The fact that distinctions between the lymphocytes and the granulocytes are of degree rather than of nature, since the lymphocytes are unquestionably amœboid, some possess granules in their protoplasm, and there is some evidence

of the occurrence of an active lymphocytosis. 4. The fact that the lymphocytes and the granulocytes (myelocytes and the granular cells of the circulating blood) develop from a common ancestor in the bone-marrow—at least, in pathological states. 5. The fact that even clinically there is no sharp dividing line between the two forms of the disease.

Rather than two forms of the disease, there are extremes of type. That atypical and transitional (intermediate or mixed) forms do occur, and while we have hitherto thought that acute leukæmia is always lymphocytic and chronic leukæmia either lymphocytic or myelocytic, trustworthy evidence has recently accumulated tending to show that acute leukæmia may be, though rarely, myelocytic. Contrary to the rule, certain of the chronic lymphocytic cases reveal a usually large number of large lymphocytes, and some of the apparently acute cases may be of the small lymphocyte type.

Fraenkel,[35] reporting 10 cases of acute leukæmia, "drew particular attention to the blood picture which he considered typical for such cases. He describes the predominating cell as varying greatly in size from that of a red blood corpuscle to those twice as large and showing every grade of transition between the two. The large cells contain voluminous nuclei which nearly fill the cell, leaving only a narrow zone of protoplasm about them. The nuclei are round or oval, but many show indentations, and some are even polymorphous. The typical small lymphocytes are much less numerous than these large elements, but are still absolutely increased above the normal. He notes further the absence of myelocytes and eosinophiles and the relative and even absolute decrease in the number of polymorphonuclear neutrophiles."

Hamman[36] reports 3 cases of acute leukæmia in which there was an increase in the large mononuclear cells (hyaline(?) cells).

The counts of the leukocytes were in the first case 111,000, of which 77 per cent. were large mononuclear cells; in the second 119,200, of which an average of 74.4 per cent. were large mononuclears in two counts, while in the third there were 958,000 leukocytes with 90 per cent. large mononuclears. He claims that it appears unjust from the evidence at hand to relegate a blood picture as distinctive as that of Fraenkel to a subgroup under the lymphocytic variety.

In the absence of any definite pathological basis our only means of classifying leukæmias is according to the blood picture. Ehrlich was the first to adopt this method, but he uses the blood picture merely as a gauge to certain anatomical seats of the disease. Evidence being in favor of the absence of such an indication, it has been proposed to replace the terms myelogenous and lymphatic by the more uncompromising ones, myelocytic and lymphocytic, which have reference to the blood picture alone.

Savory,[37] in a child aged four and a half years, who presented enlarged glands of the axilla and above the right clavicle, found upon examining the blood 35 per cent. hæmoglobin, 2,157,000 red cells, and 356,000 leukocytes. Spreads of the blood stained with hæmatoxylin and eosin showed that the red cells were practically normal, and only found two nucleated red cells while counting 611 white cells. Both were normoblasts. A differential count of the leukocytes gave: polynuclears 3.45 per cent.; large and small lymphocytes, 96.07 per cent.; eosinophiles, 0.33 per cent.; myelocytes, 0.16 per cent. "The large lymphocytes greatly predominated, but there was no line of demarcation between the large and the small; so they were counted together. The majority seem about from 12 to 14μ in diameter." Death occurred in seven weeks. No autopsy was performed.

Zypkin[38] reports a case of a woman, aged thirty-nine, in whom a first examination of the blood showed the presence of 2,700,000 erythrocytes, 8800 leukocytes, and 35 per cent. hæmoglobin. At this examination the polynuclear leukocytes were 64.5 per cent.; large lymphocytes, 22.4 per cent.; small lymphocytes, 5.4 per cent.; mononuclear leukocytes with ungranulated protoplasm, 6.4 per cent., and eosinophiles, 1.3 per cent.

Two weeks later the erythrocytes were 1,550,000; leukocytes, 106,400; hæmoglobin, 24 per cent. In this report the large lymphocytes were 64.7 per cent.; polynuclears, 11.9 per cent.; small lymphocytes, 6.3 per cent.; mononuclear neutrophiles, 2.4 per cent.; mononuclear leukocytes with ungranulated protoplasm, 14.4 per cent.; eosinophiles, 0.3 per cent. Poikilocytes, normoblasts, and megaloblasts were present. In this case there was enlargement of the spleen—four fingers' breadth—below the border of the ribs, and the observer thinks that it was primarily a splenic anæmia in which a transition into acute lymphatic leukæmia occurred.

G. S. Middleton[39] reports a case of acute lymphatic leukæmia occurring in a youth nineteen years of age which proved fatal three months after the glandular enlargement was first noticed (cervical glands). The white blood cells, though not counted in a hæmocytometer, were estimated at about 30,000 per c.mm. Large lymphocytes were 87.3 per cent.; small lymphocytes, 4.2 per cent.; polymorphonuclears, 2.5 per cent.; large mononuclears (hyaline), 6 per cent. No marrow-cells or mast-cells were observed and extremely few eosinophile cells. The red corpuscles showed a moderate poikilocytosis, but no nucleated reds were found. The number of erythrocytes and the percentage of hæmoglobin were not estimated.

Puchberger[40] claims that in leukæmia there are observed markedly hypertrophic forms of blood platelets, which sometimes attain the size of lymphocytes. When the blood is stained with brilliant cresylene blue he noticed, after the lapse of ten or fifteen minutes, the separation of a hyaline substance which, in the form of a cylin-

der, is inseparably attached to the similarly circumscribed stained substance of the blood platelet.

Wende[41] mentions a very interesting case of lymphatic leukæmia preceded by Hodgkin's disease. There was spontaneous increase and reduction of tumors, characteristic of Hodgkin's disease, with suddenly developing clinical and blood changes showing transition from pseudoleukæmia into true lymphatic leukæmia. The first blood examination gave: hæmoglobin, 88 per cent.; erythrocytes, 5,128,000; leukocytes, 4000. Differential count: lymphocytes, small, 27 per cent.; lymphocytes, large and transitional, 4 per cent.; polynuclears, 68 per cent.; eosinophiles, 1 per cent. Microblasts and microcytes were occasionally observed.

Several months later two blood examinations gave a general result as follows: hæmoglobin, 40 per cent.; erythrocytes, 1,856,000; leukocytes, 39,000; lymphocytes, small, 95.4 per cent.; lymphocytes, large, 1.1 per cent.; eosinophiles, 0.5 per cent.; polynuclears, 2.9 per cent.; myelocytes, 0.1 per cent. Microcytes, macrocytes, and poikilocytes were observed, as well as an average of 168 nucleated reds (102 in first and 225 in second) per c.mm. and a number of polychromophiles.

A streptococcus infection occurred, and just twenty-four hours before death the hæmoglobin was 30 per cent.; erythrocytes, 803-000; leukocytes, 1600, and the specific gravity 1.030. Megalocytes and poikilocytes were found, together with schistocytes; no normoblasts. The small lymphocytes were 88 per cent.; large and transitional lymphocytes, 1 per cent.; polynuclear neutrophiles, 10 per cent.; eosinophiles, 1 per cent. Infiltration of lymphocytes was more or less marked in all the organs and in the skin.

Dorothy Reed[42] cites a case of a man, aged forty-seven years, in whom the disease was preceded by a severe attack of epistaxis. The blood was examined twice, ten days and seven days before death. An enormous increase in the leukocytes was apparent, the white cells being about as numerous as the erythrocytes. No differential count was made. No general or even local enlargement of the lymphatic glands was noticed; the bronchial, peritracheal, and aortic glands, though deeply pigmented, were rather soft and translucent. The mesenteric glands were not enlarged, were deeply pigmented, grayish-yellow and translucent, and somewhat softer than normal. Along the retroperitoneal region the hæmolymph glands were very conspicuous, had a dull-red color, and were not especially enlarged.

In blood smears made from the heart at autopsy in over a thousand non-granular mononuclear cells, only three or four granular polynuclear leukocytes and four normoblasts were seen. The uninuclear cells varied from cells almost twice the size to those considerably smaller than the normal red blood cells. The nuclei were round or oval. The red cells appeared normal in size, form,

and staining properties. Nucleated cells were of the normoblast type. Section of a chicken-fat clot from the heart showed a meshwork of fibrin and entangled leukocytes, the most conspicuous of which was the lymphoid cell. In the marrow the predominating white cell was the lymphocyte; few normoblasts, but no megaloblasts, were observed. In the lymphatic glands the sinuses were engorged with lymphocytes and the follicles to a less extent. All the viscera contained small foci of infiltration of lymphocytes, but none to a marked degree. Reed suggests that "there are three forms of leukæmia, all due to myelogenous changes, and that these should be known as the myelocytic, lymphoid, and mixed-cell varieties, if we wish to make the blood picture the basis for clinical divisions."

Miller and Hess[43] report a case of acute leukæmia with death due to rupture of the spleen. The leukocytes varied from 50,000 to 161,000. An average differential count gave: small lymphocytes, 4 per cent.; large lymphocytes, 81 per cent.; eosinophiles, 3 per cent.; myelocytes, 1.5 per cent., and polynuclears, 10.5 per cent. Numerous megaloblasts were observed.

Williams,[44] in speaking upon the pathology of leukæmia, claims that there are two forms: one in which the cells are derived from the marrow (myelocytic) and one in which the cells originate mainly in the lymph glands, though also found in smaller numbers in the spleen and marrow (lymphocytic). Lymphatic is a rarer disease than myelocytic leukæmia, and the primary affection is in the lymph glands. We find these glands enlarged, whitish or grayish-white on section, and overloaded with lymphocytes. Many are decidedly larger than usual, but all are of the same type. We never find any form of marrow cells or eosinophiles in pure lymphatic leukæmia. Secondary deposits of a similar character are regularly found in the spleen and marrow and sometimes in other organs. The blood is surcharged with lymphocytes, great and small. The primary disease—leukosis—is seated in the lymph glands.

Pawlowski[45] describes a bacillus in the blood and tissues, especially in the lymphatics and blood paths of the liver, in three cases of leukæmia. He infers that the leukæmia is the reaction of the leukocytes of the blood-forming organs and to a less extent of the blood itself to the irritant bacillus. Fermi isolated a short, blunt bacillus from the spleen of a person dead of leukæmia, but failed to find it in twelve spleens in persons dead of other diseases. Kelsch and Villard[46] found and proved the pathogenic properties of the bacillus (in rabbits) discovered by Fermi.

A. Westphal[47] reports a case of acute leukæmia in which death was precipitated by a puncture of the spleen made for diagnostic purposes. At the necropsy the spleen was enveloped with a large blood clot; no large vessels were ruptured. Cultures were made from all the internal organs and fluids with negative results.

Ord and Copeman[48] discovered Charcot-Leyden crystals in the blood of a leukæmic, both before and after death, but many more after death; Westphal[49] found the same crystals in fluid drawn from the spleen during life.

Von Jaksch[50] claims that peptone can be demonstrated in the blood where disintegration is marked, as in leukæmia.

Mathes, of Jena,[51] examined the blood of 2 cases of leukæmia for peptone and allied bodies. In neither did he find peptone, but in each deutero-albumoses were demonstrable in the blood and serum.

Xanthin and hypoxanthin are present in the blood, as well as lactic and formic acids, according to Strümpel.[52]

Freund and Obermayer[53] found a notable decrease of fixed substances and a notable quantity of peptone in the blood of leukæmic individuals. Upon chemical analysis the spleen yields xanthin, hypoxanthin, glutin, glycocoll, leucin, and tyrosin. The same authority (Roberts[54]) says there is an increase in the fat and fibrin in the blood, with albukalin, mucin, and acetic acid, together with xanthin, hypoxanthin, lactic and formic acids. Bohland and Schurz[55] have determined that the excretion of uric acid is increased in leukæmia. Toulmin[56] reports 2 cases of leukæmia in negroes, one being interesting on account of a malarial history and the disappearance of leukocytosis, with diminution in size of the spleen under treatment with arsenic. Quincke[57] and Stintzing both observed a recession of the symptoms of leukæmia after the onset of general miliary tuberculosis. Engelhardt of Riga[58] records a case in which there was an attack of hæmoglobinemia, hæmoglobinuria, and icterus.

The case of lymphatic leukæmia here reported came under the observation of Dr. Julius Salinger in the Jefferson Hospital in 1900, and to whom the writer is indebted for the clinical history of the case.

The clinical notes are: K. S., aged forty-eight years, female, white, married. Mother died of tuberculosis at the age of fifty-six; father died of apoplexy at fifty-four; one brother died of tuberculosis; three other brothers also deceased, causes unknown.

In childhood the patient had measles, mumps, scarlet fever, and two attacks of diphtheria; good recovery followed all these diseases. Menstruation was first noticed when twelve years of age. The periods were painless, the flow profuse, lasting from three to seven days. One child was born to her when she was thirty years of age, and she had no miscarriages. Six years ago she had peritonitis, the attack lasting two weeks, with eventual good recovery.

Six weeks before coming under observation the patient noticed dyspnœa on slight exertion. The attack of dyspnœa was followed by severe pain, more or less periodical. This pain (dull and gnawing) was limited to an area reaching from the lower margin of the last ribs to the anterior superior spine of the ilium on the left side. Relief was obtained by assuming the prone position and when

lying on the left side. Œdema of the arms and legs followed these attacks of pain, which condition persisted for several days, leaving her in a very much weakened condition. Headache, vertigo, and impairment of vision (as of a scum over the eyes) were also prominent symptoms. Bowels were constipated, tongue coated, appetite fair.

An examination of the sputum was negative as regards tubercle bacilli. Examination of the urine resulted as follows: color, lemon yellow, clear; specific gravity, 1010; reaction, acid; albumin, a trace; sugar, none; urea, 1 per cent. Microscopic examination showed oxalate of lime crystals, amorphous urates, and a few squamous epithelial cells. No casts were demonstrable.

Repeated examinations were made of the blood, and these are appended:

June 19, 1900.	Hæmoglobin	25	per cent.
	Erythrocytes	1,000,000	
	Leukocytes	22,500	
	No differential count made.		
June 20, 1900.	Hæmoglobin	25	"
	Erythrocytes	931,200	
	Leukocytes	23,000	
	Differential count of leukocytes was:		
	Small lymphocytes	62.5	"
	Large lymphocytes	3	"
	Polynuclears	32	"
	Eosinophiles	2.5	"
July 7, 1900.	Hæmoglobin	25	"
	Erythrocytes	1,000,000	
	Leukocytes	2,500	
	Differential count of leukocytes was:		
	Polynuclears	69	"
	Small lymphocytes	23	"
	Large lymphocytes	8	"
	Eosinophiles	0	"
July 13, 1900.	Hæmoglobin	25	"
	Erythrocytes	1,240,000	
	Leukocytes	2,800	
	Differential count of leukocytes was:		
	Polynuclears	70	"
	Small lymphocytes	22	"
	Large lymphocytes	8	"
	Eosinophiles	0	"
Aug. 10, 1900.	Hæmoglobin	40	"
	Erythrocytes	1,204,000	
	Leukocytes	4,000	
	Differential count of leukocytes was:		
	Polynuclears	63	"
	Small lymphocytes	26	"
	Large lymphocytes	10	"
	Eosinophiles	1	"
	Poikilocytosis was observed in this examination.		
Aug. 16, 1900.	Hæmoglobin	35	"
	Erythrocytes	1,732.000	
	Leukocytes	111,000	
	Differential count of leukocytes was:		
	Polynuclears	5	"
	Small lymphocytes	90	"
	Large lymphocytes	5	"
	Eosinophiles	0	"

Aug. 22, 1900.	Hæmoglobin		40 per cent.
	Erythrocytes	1,672,000	
	Leukocytes	35,009	
	Differential count of leukocytes was:		
	Polynuclears		7 "
	Small lymphocytes		92 "
	Large lymphocytes		0 "
	Eosinophiles		1 "
	This count shows poikilocytosis and nucleated red cells.		
Aug. 28, 1900.	Hæmoglobin		35 "
	Erythrocytes	1,796,000	
	Leukocytes	16,000	
	Differential count of leukocytes was:		
	Polynuclears		20 "
	Small lymphocytes		79 "
	Large lymphocytes		0 "
	Eosinophiles		1 "

As a result of the blood examination a diagnosis of lymphatic leukæmia was made. The patient did not improve under treatment, but gradually grew worse, and died.

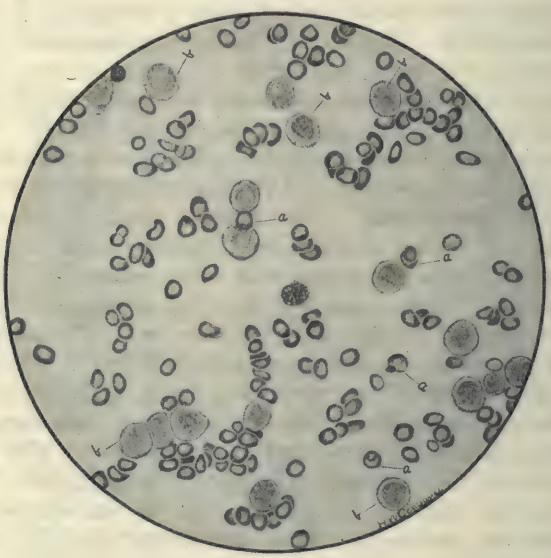
An autopsy was made, but permission was not granted to examine the nervous system. The notes of the autopsy follow: Body of a well-preserved, middle-aged female. Skin has a yellowish-brown or bronze tint, more marked and darker around the neck than any other portion of the body. Post-mortem rigidity well marked in both upper and lower extremities. Suggillation is slight in back and buttocks. Upon abdominal wall, scars, indicative of past pregnancy, are seen. Slight œdema of feet; few ecchymoses upon scalp near the forehead. The lips and gums are pale. The subcutaneous fat is well preserved; musculature reddish in color. Small epiplocele is present at umbilicus, measuring 3 cm. in diameter. Vessels of the omentum are injected; blood is still fluid. The larger vessels of the stomach are all distended and engorged. The appendix measures 10 cm. in length and is intimately bound down by mesentery. The liver extends completely over to the left side and to 5 cm. below the umbilicus. The peritoneum contains 100 c.c. of slightly cloudy fluid. The pericardium contains 100 c.c. of clear, straw-colored fluid; otherwise it is normal.

Right side of heart is dilated. The right auricle contains a large number of chicken-fat clots, together with a large quantity of fluid, watery blood. Right ventricle contains a few currant-jelly and chicken-fat clots and fluid blood; while the left auricle and left ventricle are comparatively empty. As the heart is cut from the great vessels a large number of small clots and a large quantity of blood wells out. Heart weighs 330 gms. Muscle is flabby, pale in areas, and there is an abundance of epicardial fat present. The right ventricular wall is thin, and the adipose tissue represents about two-thirds of its thickness. There is slight thickening of the tricuspid and mitral leaflets; aortic valve shows fenestration of middle leaflet; beginning atheroma of the aorta is also noticed.

Left pleura shows marked general adhesions; the lung is compressed and markedly œdematous. Weight 480 gms. Right pleura is universally adherent; the right lung is more œdematous than the left. Weight 570 gms. The spleen is large, dark red in color, measures 22 cm. by 17 cm. by 7 cm. The surface shows areas of capsulitis and the organ is adherent to the under surface of the liver. Upon section the organ cuts with slight resistance, and there is an apparent prominence of the Malpighian bodies; no amyloid reaction could be obtained. Weight 300 gms. The left adrenal shows no appreciable change macroscopically.

The left kidney is movable, enlarged, pale, and flabby, and measures 16 cm. by 3.5 cm. by 2.5 cm. and is slightly lobulated.

Fig. 1.



It cuts with some resistance. The organ is pale throughout; there is a slight increase of adipose tissue in the pelvis. The capsule strips with ease and the surface is smooth. Weight 180 gms.

The right adrenal is apparently normal.

The right kidney is also slightly movable, lobulated, flabby, and cuts with ease; the substance is pale. The capsule strips easily, leaving a smooth surface. Weight 170 gms. Both ureters are normal.

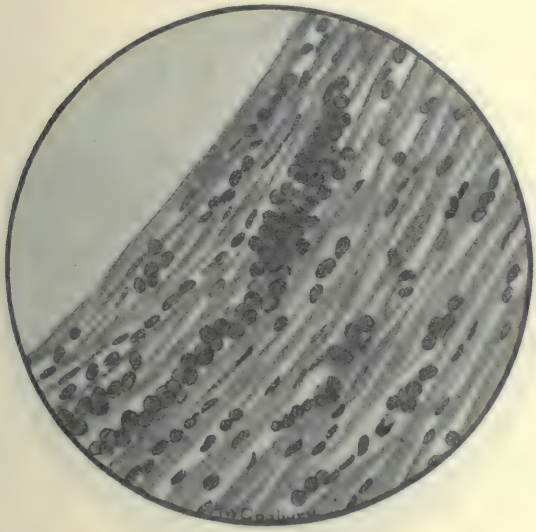
The liver, as mentioned previously, extends completely to the left side of the abdominal cavity. It measures 33 cm by 23 cm. by 9 cm. The organ is slightly paler in color than normal and cuts with slight resistance. Throughout the substance small, whitish or yellowish-white areas, more or less continuous with one another,

are seen, which do not give the amyloid reaction. The upper surface of the liver shows few areas of peritonitis. The gall-bladder is distended and contains 30 c.c. of a black, tenacious, tarry fluid. The bile-duct is patulous; no calculi in gall-bladder. Weight of liver 2800 gms.

Upon the under surface of this organ there is a large number of small masses, 1 to 5 cm. in diameter, which cut with slight resistance. Upon the cut surface (of these masses) small, pinkish-white, translucent areas 2 mm. in diameter are noticed, which do not give the amyloid reaction. These masses are apparently enlarged glands.

The uterus is normal; the left ovary is prolapsed and cystic; right ovary is atrophied. The bladder is empty and its walls are

FIG. 2.

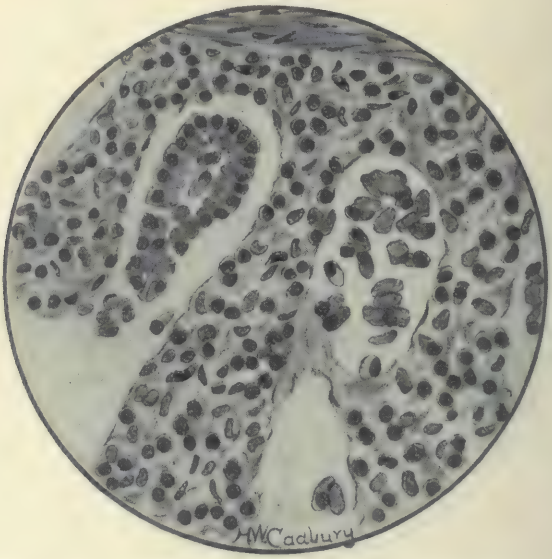


very much thickened. The stomach is apparently normal and shows the usual congestion noticed post-mortem. The pancreas measures 18 cm. by 3 cm. by 1.5 cm., and is apparently normal. Weight 95 gms. The intestines present no apparent lesions macroscopically.

Histological Examination. The musculature of the heart is swollen and slightly granular. The striations in some fibres, as well as the nuclei, have disappeared. In some areas the muscle nuclei are normal, muscle fibres are wavy or spiral, and in still others fragmentation is present. The capillaries are filled with leukocytes, few of which are finely granular oxyphiles, but mostly lymphocytes. Irrespective of the capillaries, numerous lymphocytes are found between the muscular fibres, some in single, others in double column.

In one specimen a large accumulation of these cells is seen occupying the spaces of a fragmented fibre—*i. e.*, situated between the separated ends. In another specimen areas made up of a delicate, wavy, homogeneous tissue are seen, in which are entangled lymphocytes. These areas seem to have taken the place of heart muscle destroyed by fragmentation. Very few red blood corpuscles are demonstrable, either in the capillaries or between the fibres. Numerous mast-cells or mucinoblasts are also noticeable. Oil globules, both small and large, are seen in those specimens fixed with osmic acid. A large number of slightly oval and some spindle-shaped cells (these latter being finely granular and having no apparent nucleus) are also demonstrable, especially around the capillaries.

Fig. 3.



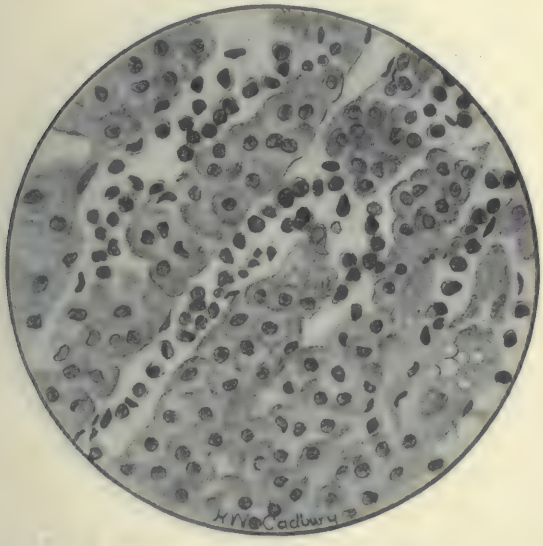
In examining the spleen the first thing that impresses the observer is the appearance of unusual cellular density of the sections. Enormous numbers of erythrocytes are seen scattered throughout; most of these are perfectly normal, exhibiting no fragmentation whatever. The bloodvessels are engorged, principally with leukocytes; some of the vessels show rupture of the coats, even those within the trabeculæ, while others show infiltration or dissection of the coats by lymphocytes. The whole splenic pulp seems to be made up of two cells—erythrocytes and lymphocytes. The Malpighian bodies are not at all prominent, and in some the small artery is infiltrated with the cells. Upon closer examination small masses of lymphocytes are seen, more or less cylindrical in shape, which correspond to leukæmic infarcts. Few mast-cells are demonstrable.

The capsule of the organ is thickened and, to some extent, infiltrated with lymphocytes, even to the extreme periphery. Despite the presence of such a large number of erythrocytes in the splenic pulp there is very little pigmentation present.

The cells of the adrenals are slightly cloudy or granular. The cortical portion of the organs are infiltrated with lymphocytes. This is most marked in the zona reticularis; the zona fasciculata shows some, while the zona glomerulosa shows the least infiltration. In the medullary portion there is no appreciable alteration. The small quantity of adipose tissue surrounding the adrenal is also infiltrated with lymphocytes.

The left and right kidney show cloudy swelling, the nuclei of some of the cells being distinctly visible, others showing an entire

Fig. 4.

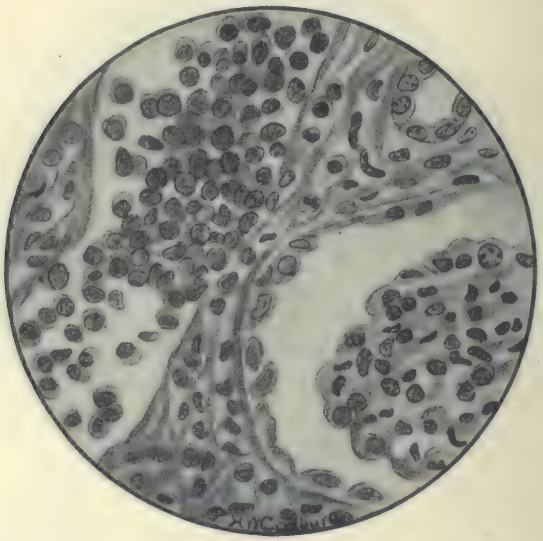


absence of nuclei. The protoplasm is distinctly granular; in some tubules only granular débris is present. Large areas of cellular infiltration are noticeable between the tubules, and to some extent obliterating them. At first glance one might think it was an area of acute infection, but upon closer examination the cells are found to be for the most part lymphocytes. Together with these is a large number of slightly granular, spindle-shaped cells which resemble those found in the heart. Besides the large areas of cellular infiltration mentioned above, single and double columns of lymphocytes are seen between the collecting tubules. The capsule of Bowman is also infiltrated with lymphocytes.

The liver shows an extensive and marked cloudy swelling of the parenchyma, the nuclei being for the most part entirely obscured

or very faintly outlined. Between the columns of cells throughout the entire organ are lymphocytes which encroach to such a marked degree upon the liver substance that a certain amount is destroyed. Small and large aggregations of lymphocytes are seen (irrespective of those between the cells), some circular in outline and others irregular, which correspond to leukæmic infarcts. These are visible to the naked eye. There is a slight degree of fatty infiltration present, but no evidence of a cirrhotic process. Under a higher magnification the liver substance appears more or less in islands, and together with the lymphocytes mentioned quite a few red blood cells are seen between the rows of liver cells. Histologically the pancreas is comparatively normal, showing only a few lymphocytes around the bloodvessels.

Fig. 5.



Examination of the intestine shows marked lymphocytic infiltration between the crypts of Lieberkühn and in the villi. There is no evidence of ulceration, but the enormous number of lymphocytes resembles very closely areas of infection. In the submucous and muscular coats large numbers of mast-cells are demonstrable, especially in the former. There are also a few of these cells seen in the villi. The bloodvessels are dilated and filled with lymphocytes.

The peribronchial and mesenteric glands show such an increased density that the typical arrangement is destroyed. There is also a certain amount of pigmentation present in the former. Few mast-cells are demonstrable.

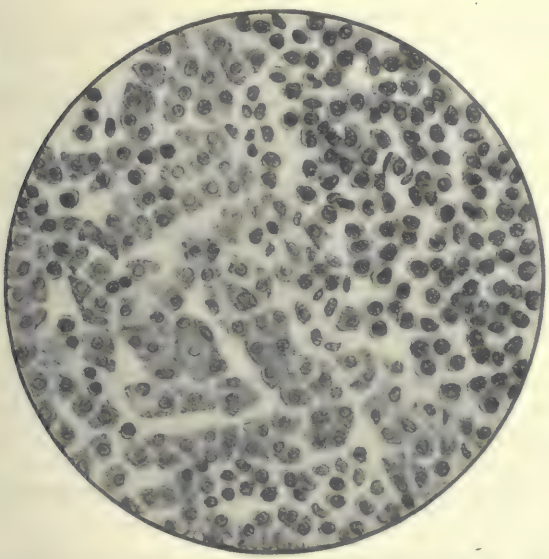
There is no apparent increase in the elastica in any of the organs examined.

The bone-marrow of the ribs is extremely pale and scant. The cancellated structure is distinctly dry. Spreads made from the marrow contain lymphocytes and a few red blood cells, the latter mostly in islands. An occasional myelocyte and hyaline cell are seen. A few nucleated red cells are demonstrable, some exhibiting extrusion of the nucleus.

Spreads made from the heart's blood, spleen, and liver show exactly the same cellular elements as those from the bone-marrow.

Some granules of the polynuclear leukocytes and lymphocytes give the iodophilic reaction.

FIG. 6.



Inoculations were made from the bone-marrow, liver, spleen, kidney, and blood upon agar, blood serum, blood-smeared agar, and acid agar. From the bone-marrow and blood a bacillus which resembled the bacillus coli communis, morphologically, tinctorially, and biologically, was obtained. From the liver no growth was demonstrable at the end of twenty-one days. From the spleen a diplococcus (which corresponded morphologically and tinctorially to the diplococcus of Sternberg) and the staphylococcus pyogenes aureus were isolated. From the kidney the bacillus pyocyaneus and staphylococcus pyogenes aureus were obtained.

The case is interesting on account of its rarity and the comparatively short duration of the illness. All the organs examined except the pancreas show the lymphocytic infiltration to a marked degree. The infiltration of the peribronchial glands and conse-

quent enlargement would, no doubt, account for the dyspnœa. The bacterial findings apparently indicate an agonal infection.

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EXPERIMENTAL ARTHRITIS AND ENDOCARDITIS PRODUCED BY A STREPTOCOCCUS ISOLATED FROM THE BLOOD OF A CASE OF RHEUMATISM, ENDOCARDITIS, AND CHOREA.[1]

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Although rheumatic fever is believed by many to be an acute infectious disease, the specific agent concerned in its causation has been widely disputed, and even at present few authorities are agreed as to its etiology. The symptomatology, the frequent association with endocarditis, and the unique character of the disease have always suggested that rheumatic fever was due to some bacterial infection, and, therefore, it is not surprising that most of the investigations regarding its etiology should be carried out with this thought in mind. The results of many of the earlier studies were confusing and often contradictory, but certain recent investigations, coming especially from Germany and England, seem to throw some light upon the problem.

The intimate relationship between chorea and rheumatism,[2] and the artificial production of chorea by intravenous inoculation of a diplococcus from a case of rheumatism, as claimed by Beattie, to be referred to later, makes this subject doubly interesting.

In much of the earlier work done by Sahli,[3] Singer,[4] and others cultures from the blood, urine, and joint fluid of cases of rheumatic fever frequently yielded not one but several types of bacteria. Among these staphylococci, streptococci, and even certain bacilli belonging to the colon group were described. Experimental inoculations proved the virulence of these bacteria, but arthritis and endocarditis could scarcely if ever be reproduced. Contradicting these observations were the results reported by Chvostek,[5] and Kraus,[6] who could not obtain any growth of bacteria in cultures from the blood, joint fluid, or urine. In 1897 Achalme[7] published

[1] Read before the Association of American Physicians, Washington, May 11, 1904.

[2] Lewis, Seasonal Relations of Chorea and Rheumatism, The American Journal of the Medical Sciences, September, 1892.

[3] Deut. Arch. f. klin. Med., 1892, Bd. li. p. 451.

[4] Aet. u. Klinik des akuten gelenk rheumatismus, 1898, Leipzig, Verhandl. des XIX. Cong. f. inner Med., 1901, p. 441; Wien. klin. Woch., 1901, No. 20.

[5] Wien. klin. Wochen., 1895, No. 26, p. 469.

[6] Zeit. f. Heilkunde, 1896, Bd. xvii.

[7] Annal de l'Inst. Pasteur, 1897, p. 845; Gaz. méd. de Paris, 1901, No. 14, p. 105.

an account of his work with a spore-bearing anaërobic bacillus which he had previously described in 1891. This organism was cultivated from the blood of cases dying of acute articular rheumatism. The bacillus grew best in milk. Inoculations into animals produced spreading hemorrhagic phlegmons and general septicæmia. The later work of Menzer and others goes to show, however, that this organism may be obtained from the bodies of cadavers or even from milk which is not overcarefully sterilized, the spores being very resistant to heat. Walker considers that this organism is bacillus enteritidis sporogenes.

Wassermann,[1] in 1899, described a diplococcus or streptococcus which he obtained in cultures from the heart's blood and endocardial vegetations of a child dead of rheumatism, endocarditis, and chorea. This diplococcus developed in the ordinary culture media exactly like streptococcus pyogenes, but produced the most remarkable lesions in animals. A series of successive intravenous inoculations into eighty rabbits showed that it was possible to set up a multiple arthritis which rarely proved fatal. The joint symptoms occurred with great regularity, and developed only after an incubation period of three to six days. Frequently the infection spread from one joint to another. Soon these results were confirmed by Triboulet,[2] in France, who was able to produce in some of his rabbits endocarditis, pericarditis, and pleurisy. Later, Menzer[3] and Meyer[4] obtained streptococci from the throats of patients suffering from rheumatic angina. These organisms were characterized principally by their power of producing multiple arthritis in rabbits. The joint lesions occurred constantly, and were often associated with a vegetative endocarditis. Singer[5] somewhat later announced that the streptococcus which he had previously described was identical with the organism obtained by these observers.

In England the extremely severe type of rheumatic fever has afforded an excellent field for the study of this disease, and the results obtained by English observers have, perhaps, been more striking than those reported from other countries. Poynton and Paine,[6] since their first publication, in 1900, have isolated a diplostreptococcus from twenty-two cases of rheumatic fever. The organism was obtained occasionally from the blood before death in severe cases, but usually from the blood, endocardial vegetations,

[1] Berl. klin. Wochen., 1899, No. 29, p. 638.

[2] Compt.-rend. de la Soc. de Biolog., 1898, v. p. 124; Gaz. des hôp. des Paris, 1902, t. lxxv. p. 1439; ibid., 1903, t. lxxvi. p. 405.

[3] Aet. des akuten Gelenkrheumatismus, Berlin, 1902.

[4] Zeit. f. klin. Med., 1903, Bd. xlvi. p. 311; Verh. des XIX. Cong. f. inn. Med., 1901, p. 452; Verh. des Vereins f. inn. Med., January 7, 1901.

[5] Loc. cit.

[6] Lancet, 1900, vol. ii. p. 861; British Medical Journal, 1901, vol. ii. p. 779; Medical Press and Circular, 1903, vol. cxxvi. p. 478.

and complicating lesions after death. Intravenous inoculation into rabbits was followed by an interesting train of lesions. Monoarthritis and polyarthritis was an almost constant result, while endocarditis, pericarditis, and pleurisy were occasionally encountered. The organism could be cultivated from the joints and endocardial growths of the animals. Among other lesions subcutaneous fibroid nodules were described in which the particular diplococcus could be demonstrated. Definite chorea could never be reproduced in any of the animals. Poynton and Paine consider that this organism is identical with that described by Wassermann and Triboulet, and believe that it is the specific cause of rheumatic fever. Recently Ainley Walker[1] and Walker and Beaton[2] have fully confirmed Poynton and Paine's results. They were able to cultivate a diplococcus from fifteen cases, including acute rheumatism, rheumatic endocarditis, pericarditis, chorea, and endocarditis. Intravenous inoculations into animals produced monoarthritis and polyarthritis, pericarditis, endocarditis, septicæmia, and death. Beattie[3] claims to have produced chorea as well as endocarditis and arthritis in rabbits inoculated intravenously with a diplococcus obtained at autopsy from the knee-joint of a case of rheumatic fever. Finally, Shaw[4] has made a comparative study of the cocci isolated by Wassermann, Poynton and Paine, and Walker. He finds that these various bacteria produce practically the same effects when inoculated into rabbits and monkeys, and may give rise to endocarditis, pericarditis, myocarditis, arthritis, pleurisy, and iritis.

In America almost no work had been done on this subject. Dana,[5] in 1894, found diplococci in sections of the meninges of a child dead of chorea, but since cultures were not made the character of this organism must remain in doubt.

The recent papers of Poynton and Paine, Walker, and Menzer deal quite extensively with the literature upon the subject. In view of the interesting experiments which have been made in England and Germany it was thought advisable to record the following case of rheumatism, endocarditis, and chorea.

M. H., female, aged eight years, admitted into the Orthopædic Hospital and Infirmary on October 15, 1903, under the care of one of the writers, with the following history furnished by Dr. W. T. Skinner, of Glasgow, Delaware:

"Toward the latter part of August or early part of September, 1903, the child was taken sick; she had fever and was confined to bed with a swollen and painful ankle. Under salicylate of soda

[1] Practitioner, 1903, vol. lxx. p. 185.
[2] British Medical Journal, 1903, vol. i. p. 237; ibid., vol. ii. p. 659.
[3] Journal of Pathology and Bacteriology, 1904, vol. ix. p. 272.
[4] Ibid., 1903, vol. ix. p. 158.
[5] The American Journal of the Medical Sciences, 1894, vol. cvii. p. 31.

the child rapidly improved, and was able to run about and play. Although she had relief from pain and swelling, she did not appear to be well, and was languid. She was given quinine in tonic doses, and was not seen again until toward the end of September, when she began to exhibit choreic movements, which were particularly noticeable in her hands, feet, and face, and not unilateral; she also now complained of stiffness and soreness of the wrists. Three days later, September 29th, the movements had become so severe that the child could not swallow, and the sides of the bed had to be padded to prevent her injuring herself in her violent movements."

This condition continued until brought to the Infirmary on October 15th.

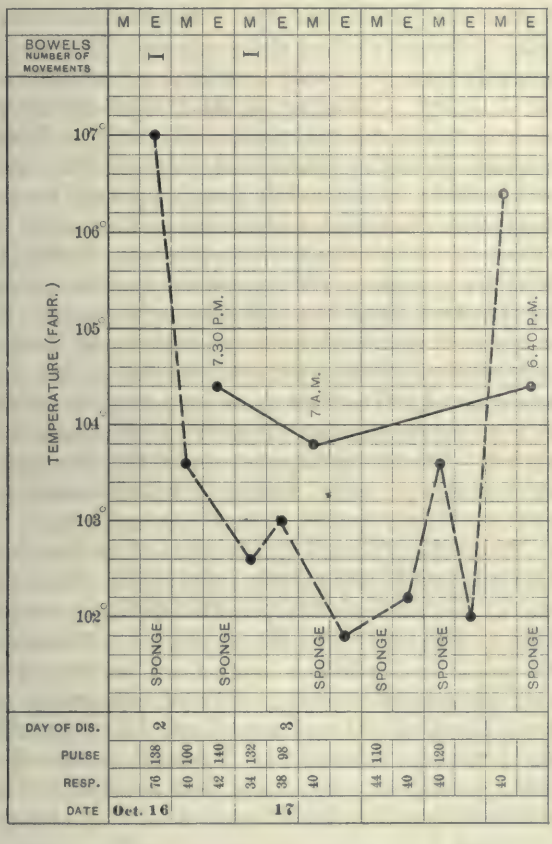
Upon admission, at 5 P.M., after a journey from Delaware, the child was perfectly limp and with but very slight choreic movements. She was unable to voluntarily move hand or foot, and the limbs hung as if paralyzed. She could not speak, and scarcely even swallow. The temperature was not taken, but the child seemed entirely apyretic. No heart murmurs could be detected. Pulse and respiration were both very rapid, and the latter shallow. On the morning of the 16th her temperature suddenly rose to 107°, and the choreic movements were excessive and so violent as to necessitate the padding of the sides of the crib. Her respirations were 76 per minute, and her pulse was 138.

Under sponging and chloral by mouth and rectum the temperature rapidly fell, becoming 101° F. by the morning of the 17th; the movements still, however, remained severe. Arsenic was first administered by the mouth and later hypodermically. No cardiac murmurs could be heard on the 16th, although they were carefully sought for, but on the morning of the 17th a soft apex systolic murmur was detected, which rapidly increased in intensity until her death, on the evening of the 17th, with a second rise of temperature to 106.5°. A blood culture was made on the afternoon of the day of her death. Although the greatest care was taken, the constant agitation was beginning to cause abrasions of elbows, shoulder-blades, hips, and heels. No examination of the urine was made, as none could be collected without catheterization, owing to the violent movements. No autopsy was allowed.

The accompanying chart shows the course of the fever.

Cultures were made from the median basilic vein about twelve hours before death. Three c.c. of blood were drawn with aseptic precautions and put into two flasks, one containing about 250 c.c. of litmus milk and the other about 250 c.c. of bouillon, to which 10 c.c. of hydrocele fluid had previously been added. After forty-eight hours the milk flask showed a marked acid reaction. The bouillon flask did not show any growths. Cover-slips from the milk flask revealed a small delicate diplococcus which occasionally formed chains of short length. The organism was immediately plated.

In agar plates both surface and deep colonies were exactly like those of streptococcus pyogenes. The morphology of the organism was that of a delicate diplococcus growing often in long chains in fluid media. Gram's stain was held, provided the decolorization in alcohol did not last more than two to three minutes. On plain agar slants the growth was exceedingly delicate and sparse. Separate tiny gray pinpoint colonies were scattered over the surface. On hydrocele agar the growth was somewhat more luxuriant, while



the condensation water showed marked clouding. On plain agar the cultures died within a week or ten days, but on hydrocele agar slants they could readily be kept alive for two to three weeks. This medium was, therefore, used entirely for the transplantation of the stock cultures. Milk was rapidly acidified and often clotted after a week's growth. In bouillon there was a scant growth collected in minute granules at the bottom of the tube. If, however, the reaction was alkaline (—10 Eyre) the growth was heavier. A growth could always be obtained in gelatin. There was no liquefaction.

On October 22d, five days after the organism had been isolated, two rabbits were inoculated intravenously with suspensions made with bouillon from a twenty-four-hours' growth on two hydrocele agar slants. Rabbit I. received 2 c.c. Rabbit II. received 1 c.c. On October 25th, three days after inoculation, both rabbits seemed well.

26th. Rabbit I. lies quite still and seems sick. When disturbed it moves about with difficulty and appears to drag right hind leg.

November 11th. Rabbit I. has remained definitely lame in left hind leg. Left ankle-joint is swollen. Hops about with a good deal of difficulty. Rabbit II. has also been quite lame in hind legs, but has apparently recovered, and now hops about with moderate ease. Rabbit I. killed. At autopsy 30 c.c. of cloudy port-wine colored fluid was found in the peritoneal cavity. Both pleural cavities contained clear, straw-colored fluid. The spleen was rather large. The liver, kidneys, and lungs appeared normal. The heart was large and distended with blood. The walls were thin and cavities dilated. The muscle was quite soft, friable, pale, and mottled with yellow patches. All the valves appeared normal.

The right ankle was about the size of a large cherry. The surrounding tissues were not involved. When the joint was opened a thick pultaceous creamy fluid escaped, but was mixed with some cloudy glutinous fluid. The left knee was slightly swollen, and when incised a moderate amount of thick, semitranslucent, glutinous fluid escaped. The left ankle was much like the right, except that the joint was not so much swollen. All the other joints appeared normal.

Cover-slips from the affected joints showed a few leukocytes, stringy mucoid material, phagocytic epithelioid cells, and many diplococci usually within leukocytes. The diplococci stained well in gentian violet, and were not decolorized by Gram's method. Cultures were made on hydrocele agar from heart's blood, liver, spleen, kidney, peritoneal cavity, right and left ankle, and right and left knee. None of the cultures showed any growth except those from the right and left ankles. From these two situations a meagre but pure growth of streptococci was obtained. The organism on subcultures agreed in every respect with the streptococcus previously described.

A third rabbit was inoculated with the organism obtained from the right ankle of Rabbit I. Three c.c. of a suspension of twenty-four-hours' hydrocele agar culture in bouillon were injected into the ear vein. For three or four days the animal appeared perfectly well. After this time he gradually became lame in the hind legs, and eight days after inoculation the left knee appeared definitely swollen. This was followed by involvement of the right ankle, and later by slight swelling of the joints of the forelegs. The animal rapidly grew much worse, and finally died eleven days after inocula-

tion. At autopsy extensive friable vegetations were found upon the mitral valve; there was an enlargement of the spleen, with anæmic infarctions of both that organ and the kidneys. Both ankles were greatly swollen and contained pultaceous material and sticky, glutinous fluid. There was a varying amount of involvement of the right knee and hip, left knee, right wrist, elbow, and shoulder, left shoulder and left wrist. A delicate diplococcus was found in cover-slips from the mitral vegetations in enormous numbers, and from the heart's blood and all the affected joints. The organism was grown from the heart's blood, mitral vegetations, spleen, liver, kidney, right ankle, knee, wrist and elbow, and left wrist. It proved to be a streptococcus identical with the one obtained from Rabbit I. and from the original blood culture.

A fourth rabbit was inoculated in the same way as the others, with 2 c.cm. of culture. About six days after inoculation the primary symptoms of lameness and difficulty in movements developed. Although the rabbit rapidly grew very lame and appeared quite ill, no definite swelling of the joints could be made out. The animal died nine days after inoculation. At autopsy practically every joint in the body showed some swelling and contained a moderate amount of thick, glutinous fluid. None of the joints were greatly increased in size, but some showed much more swelling than others.

Cover-slips from the right and left ankles, right shoulder, right and left elbow, and left wrist showed varying numbers of polymorphonuclear leukocytes and epithelial cells, but always quantities of diplococci, usually within cells. Cultures were made on hydrocele agar from the heart's blood, right and left ankle, and left wrist, and on plain agar slants from the liver. Colonies developed only on the tubes from the joints. The cultures from heart's blood, spleen, and liver showed no growth.

Finally, a fifth rabbit was inoculated intravenously in exactly the same manner as the others, with 1 c.c. of a twenty-four hours' hydrocele agar culture. The rabbit did not appear definitely ill for nine days, but by this time it was hopping about with difficulty, seemed ill, and preferred to crouch in a corner of the cage. On December 12th the animal appeared generally in better condition, but was still lame, and definite swelling of the left ankle-joint could be made out. After twenty-five days both ankles had become swollen, though the animal seemed generally better. The animal was killed on the twenty-fifth day after inoculation.

The peritoneal, pleural, and pericardial cavities were normal. The heart, spleen, liver, and kidneys did not show any marked pathological change. On the right ankle the Achilles bursa was found to be swollen to about the size of a cherry, while there was slight increase in the size of the ankle itself. The left ankle was very extensively swollen. All the joints were normal except the right wrist. Although this joint itself was not swollen, over one of

the extensor tendons there was a firm, rounded nodule about the size of a grape seed. On section a minute central soft point was seen. Cover-slips from this soft material showed a few leukocytes and epithelial cells, while here and there diplococci were occasionally found.

The organism was only recovered from the right ankle-joint.

A microscopic study of the organs from the four rabbits revealed the following conditions:

The heart muscle showed moderate grades of fatty degeneration, with swelling and parenchymatous degeneration of muscle fibres. In Rabbit III., which died of acute endocarditis, there were accumulations of small round cells and areas of polymorphonuclear leukocytic infiltration.

In one case there were areas of focal necroses in the liver. In the spleen and kidney of Rabbit III. definite anæmic infarctions were seen, while in the latter organ many of the small vessels and glomerular capillaries were plugged with masses of diplococci.

The synovial membrane from the joints, showing various degrees of involvement, presented marked pathological alterations.

In the earlier stages there was extreme œdema, congestion, and slight infiltration of polymorphonuclear leukocytes and small round cells. In the latter stages the cellular infiltration was more intense, and the fixed connective cells showed active proliferation. Epithelioid cells and small round cells were very numerous. The surface of the membrane was covered with polymorphonuclear leukocytes and granular débris. In one section many of the vessels of the synovial membrane were completely occluded by thrombi composed of fibrin, red blood corpuscles, and leukocytes.

Great numbers of diplococci could readily be demonstrated in sections stained by the Weigert-Gram method.

To sum up, we have a streptococcus isolated before death from the blood of a case of chorea, endocarditis, and rheumatism. This streptococcus is moderately virulent for rabbits when injected intravenously, and gives rise with the greatest constancy to a multiple arthritis which is rarely fatal, unless, as in one case, it is complicated by an acute vegetative endocarditis. The onset of the joint symptoms is only noticeable after a more or less definite incubation period of four to nine days. Before this time the animals appear perfectly well. The joint involvement usually starts with swelling and tenderness in the ankles. Probably there is pain, too, for the rabbits move but little and limp when made to hop about. The infection may remain localized or spread to practically all the joints in the body. Small swellings may also develop upon the muscle tendons. The streptococcus can be recovered with great regularity from all the affected joints.

The organism, from its morphological and biological properties, could not with any certainty be differentiated from the usual varieties of streptococcus pyogenes.

Walker has emphasized the fact that the "micrococcus rheumaticus" grows readily in filtered cultures of streptococci from sources other than rheumatic fever. Marmorek believes that by this procedure various closely allied species of bacteria may be separated.

We found that the particular streptococcus under observation grew fairly well in filtered twenty-four-hours' bouillon cultures of streptococci from several sources, but occasionally it happened that streptococci from the blood of puerperal septicæmia or other sources gave the same result. This particular biological test was, therefore, thought unreliable. The interesting fact was pointed out by Walker[1] that the micrococcus rheumaticus when grown in alkaline bouillon is capable of producing large quantities of formic acid, whereas other streptococci form very small amounts of this acid. In this connection the same author has found that formic acid is present in the urine of patients suffering from rheumatic fever. When our organism was grown in bouillon (—10 Eyre) for six to eight days, and subsequently distilled with sulphuric acid, formic acid could be demonstrated in the distillate.

But in spite of these minor variations the fundamental resemblance culturally is very close between streptococci isolated from the blood or lesions of rheumatic fever patients and streptococci from other sources. On the other hand, the results of animal experiments seem to bring out possible differences.

The streptococci that have so far been described in rheumatic fever show a remarkably constant and uniform predilection for the joints, heart valves, and serous membranes of the animals into which they are injected. Wassermann[2] produced joint lesions in eighty consecutive rabbits. Meyer[3] has found fungating and vegetative endocarditis in a surprisingly large number of animals after intravenous inoculation of streptococci obtained from the throat in rheumatic angina, while Poynton and Paine,[4] as well as Walker,[5] have observed monoarthritis and polyarthritis, endocarditis, pericarditis, and pleurisy in their animals. In our own cases the mode of onset, the joint lesions themselves, and the endocarditis were most striking. In every instance the lesions show such little variation and are so constant that they must attract attention. It is also worthy of note that, though the organism be passed through several animals, the virulence is little altered.

Experiments regarding the pathogenicity for animals of streptococci from sources other than rheumatic fever are not very numerous. This portion of the question we were, unfortunately, unable to investigate owing to the difficulty in securing the large number of rabbits which would be necessary for such work. Meyer found that with attenuated cultures of certain streptococci

[1] Loc. cit. [2] Loc. cit. [3] Loc. cit.
[4] Loc. cit. [5] Loc. cit.

joint lesions could be produced in animals. This result was, however, not constant. With small doses the joints became swollen, and later went on to suppuration, the condition finally ending in death. With large doses a septicæmia, sometimes attended with joint symptoms, was observed. Glaser[1] has also observed multiple arthritis in rabbits following intravenous injections of various strains of streptococci. Under ordinary circumstances intravenous inoculations of the lower animals with virulent streptococci give rise to a rapidly fatal septicæmia, but if cultures of attenuated cocci are injected either a monoarthritis or polyarthritis may follow. The latter result is variable.

A spontaneous endocarditis following intravenous inoculations of streptococci is perhaps even rarer than arthritis. Weichselbaum,[2] in a series of experiments, found it necessary to injure the heart valves before vegetations could be obtained, and although Pasquale[3] was able to produce subcutaneous abscesses, general septicæmia, hemorrhagic infarctions of the lung, phlegmonous œdema, and hydropericardium in thirty-eight rabbits after subcutaneous and intravenous injections of streptococci from many different sources, he does not mention the occurrence of either arthritis or endocarditis. Widal and Bezancon[4] obtained a streptococcus from the mouth which gave rise to acute endocarditis in a rabbit after subcutaneous inoculations. In ninety-five experiments made with other streptococci this result was not again met with.

One noticeable feature of all these observations is the variation which many of these organisms show in their virulence for men and animals. Streptococci which produce fatal septicæmia in human beings may show very slight virulence for animals, while organisms grown from local abscesses may be rapidly fatal for animals.

In view of the fact that streptococci isolated from sources other than the blood or complicating lesions from cases of rheumatic fever do, under certain circumstances, produce arthritis and endocarditis in animals when injected intravenously, it is surprising that the English observers, particularly, have made so few experiments to control their work. This side of the question needs to be thoroughly investigated before definite conclusions can be drawn as to the specificity of the streptococcus described as the cause of rheumatic fever. Indeed, several observers, among others Menzer,[5] believe that rheumatic fever is caused not by a specific coccus, but by many varieties of streptococcus.

Most observers are agreed that it is impossible to obtain a growth of bacteria either from the blood or joint fluids of cases of rheumatic

[1] Verhandl. des XIX. Cong. f. inn. Med., 1901, p. 471.
[2] Ziegler's Beiträge, 1889, Bd. iv.
[3] Ibid., 1893, Bd. xii. p. 433.
[4] Le semaine méd., 1894, p. 195.
[5] Loc. cit.

fever which recover. Phillip[1] has recently reported such a series of negative results, and in the cases of rheumatic fever reported from the Johns Hopkins Hospital by McCrae[2] cultures from the blood and joint fluids never gave a growth of streptococci. Except in the fatal case reported we have had the same experience at the Pennsylvania Hospital. One must not overlook, therefore, the possibility of a streptococcus infection supervening as a terminal event in the fatal cases of rheumatic fever. Under these circumstances the condition might be similar to that which one finds in scarlet fever and variola.

SUMMARY. In a fatal case of rheumatism, endocarditis, and chorea a streptococcus was isolated from the blood before death. This organism did not differ materially from the common varieties of streptococcus pyogenes in cultural properties, but produced very characteristic lesions in rabbits when injected intravenously. Such inoculations were always followed after a few days' incubation period by a multiple arthritis which usually started in the ankles. In one rabbit extensive vegetations were found on the mitral valve, while typical infarctions were seen in the spleen and kidney.

We believe that this streptococcus is the same as that described by Wassermann, Meyer, Poynton and Paine, and Walker, and considered at least by the last three observers to be the specific cause of rheumatic fever.

OPERATIONS FOR PRIMARY CARCINOMA OF THE LIVER.

REPORT OF A CASE WITH FREEDOM FROM RECURRENCE AT END OF SIXTEEN MONTHS.[3]

BY LEONARD FREEMAN, M.D.,
OF DENVER, COL.

PRIMARY carcinoma of the liver is a rare affection, Hansemann finding it but six times among 258 hepatic tumors reported from the Berlin Pathological Institute from 1880 to 1889; while Eggel computes, from various sources, that it occurs about once in every 2000 autopsies. In 800 operations upon the liver, Kehr encountered but one operable cancer.

It is either nodular or diffuse (carcinomatous cirrhosis), the former variety being much more common than the latter. The

[1] Deutsch. Arch. f. klin. Med., 1903, Bd. lxxvi. p. 150.
[2] American Medicine, August 8, 1903.
[3] Read before the American Surgical Association, St. Louis, June 16, 1904.

nodules may be single or multiple, large or small. According to most observers, primary carcinoma is more apt to exist as a single nodule, although there is difference of opinion on this point.

The single primary nodule is alone amenable to surgical treatment. It may occur in any portion of the liver, but is usually found near the inferior border of the right lobe. It is generally met with during the "cancer age," but may be seen in younger individuals, a number of cases having been reported in patients under twenty years. It may arise from the endothelial lining of the bile-ducts or from the hepatic cells themselves, the latter origin being demonstrated by the secretion of bile in metastatic nodules. Metastases are common. There is almost always more or less coexisting cirrhosis of the liver. Whether the cancer arises from the cirrhosis or the cirrhosis from the cancer is still a disputed question.

There is a very close relation between tubular adenomata and primary carcinomata. They often co-exist in the same tumor; and where a numbr of nodules are present, some may be adenomata and others carcinomata, while others are in a stage of transition. Some writers, such as Terrier and Auvray, class the adenomata as adenocarcinomata, their malignancy being indicated by the metastases which frequently take place.

The only hope for permanent cure of primary carcinoma lies in early operation; but the diagnosis at this time is extremely difficult, owing to the small size of the tumor and the frequent insignificance or even total absence of symptoms. Generally, when the tumor is large enough to be felt from without, or when icterus or ascites has appeared, it is too late for an operation to be of service, except for purposes of palliation.

Statistics are difficult to obtain, especially with the limited literature at the writer's command. In 1901 Terrier and Auvray collected 52 operations for hepatic tumors. Of these 9 were primary carcinomata and 1 secondary. Ten of the 52 cases died, $19\frac{2}{3}$ per cent. Local or general recurrence has been the rule, but there are some exceptions which afford encouragement for further efforts. For instance, one case (Schrader) was well at the end of seven years, and another (Terrier) at the end of five months. A favorable case reported by Lücke, in 1890, however, was probably a gumma (Kehr) and should not be considered in this connection.

Methods of Operating. There are two principal methods of operating, both of which have numerous advocates: one in which the stump of the liver is sunk in the peritoneal cavity, and the other in which it is fastened in the wound, thus rendering it extraperitoneal, as was formerly done in hysterectomy. Owing to recent improvements in technique, the former procedure is as free from danger of hemorrhage as the latter, and is certainly preferable from the standpoint of asepsis and rapid and satisfactory

convalescence. In addition, there are cases in which the liver cannot be mobilized sufficiently to permit of secure extraperitoneal fixation, even by attaching it to the peritoneum alone—the "funnel method" of Riedel.

In case the extraperitoneal method is adopted, however, there are three ways of proceeding:

1. The operation may be done in two stages. In the first, the portion of liver containing the tumor is sutured into the abdominal wound, where it is permitted to remain until firm adhesions occur; and in the second the tumor is removed. This suggestion of Tillmanns, it may be remarked, has not been generally adopted.

2. The liver may be fastened in the wound by sutures, or possibly by needles passed through its substance, and surrounded by an elastic ligature, which remains until gangrene appears, when the dead part, including the tumor, is cut away (Lücke, Terrillon). It would seem, however, that the danger of sepsis during this time must be considerable, to say nothing of other objectionable features.

3. After securing the liver in the incision, the tumor may be excised at once.

Incision. No special form is indicated. It can be vertical or transverse, along the costal margin, or curved according to Bevan; but it should be so situated as to expose the tumor to the best advantage and afford plenty of room. It may occasionally be necessary to resect the cartilages of the eighth to the eleventh ribs (Lannelongue), or even to turn up a flap from the chest wall (Micheli), or mobilize the liver by dividing the ligaments which suspend it (Langenbuch).

Hæmostasis. After exposing the tumor the remainder of the operation consists practically in the control of hemorrhage, the actual excision of the growth usually presenting no serious difficulties. The fear of uncontrollable bleeding has greatly retarded the advancement of hepatic surgery, and it is only within the last few years that methods have been devised which have inspired a reasonable amount of confidence.

Experience has shown that no matter what precautions have been adopted, it is wise to reinforce them with ample gauze packing, especially when the cut surface of the liver is replaced within the abdomen. Failure to do this has led to disaster from delayed hemorrhage.

Numerous suggestions have been made regarding the control of bleeding during the operation and subsequently. No one of them is entirely satisfactory, but several are sufficiently so to justify their use. The principal methods are as follows:

(*a*) *Temporary Hæmostasis.* 1. Constriction of an entire lobe of the liver by an elastic ligature. This is particularly applicable to a movable left lobe, although Israel has succeeded in applying

it in a single instance to the right lobe during the removal of a sarcoma in a child.

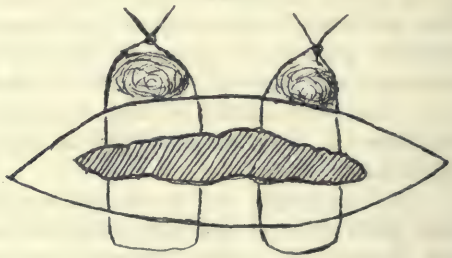
2. Digital compression furnished by assistants. This can be resorted to in favorable cases only—where the tumor is pedunculated or fairly well isolated near the border of the liver.

3. Provisional ligature of the vessels in the hepaticoduodenal ligament. This was suggested by Langenbuch, but I am not aware that it has been employed by others.

4. Parenchymatous injections of adrenalin chloride (Gualdrini). If this has any appreciable effect, it can be upon the smallest vessels only, and therefore its value seems questionable.

(*b*) *Permanent Hæmostasis.* 1. The liver may be sutured into an incision parallel to the costal margin in such a manner that the edges of the wound exert sufficient pressure to check bleeding (Chapot-Prevost). This is perhaps best accomplished by means of several mattress sutures passing through the tissues at the border of the ribs, deeply through the liver, and out through the abdominal wall below. They are then returned in reverse order and tied over compresses at their points of insertion (Fig. 1).

FIG. 1.



2. Sutures of heavy silk may be inserted through the abdominal parietes, passed under the bleeding points in the liver, brought out again, and tied on the surface of the skin (Ullmann).

3. The actual cautery. This has often proved unreliable and should not be trusted to alone, although it may be valuable in checking mere oozing.

4. Cauterization with steam at 70° C. (Caponago), or heated air (Abramowitsch). Although both these methods have been highly spoken of, they are probably no more effective than the actual cautery and not nearly so convenient. They are not frequently employed.

5. Compression by gauze is very valuable as an adjunct to other procedures, and should always be resorted to. In order to hold the gauze securely in place it may be advisable to fasten it with sutures (Hochenegg), or even to sew it between the edges of an incision.

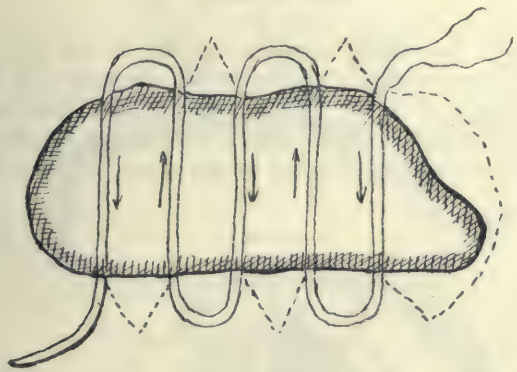
6. Immediate suture of an incised wound is ideal, but seldom practicable.

7. In order to prevent ligatures from tearing through the friable substance of the liver, an accident much feared before the experiments of Kurznezow and Pensky, Delbet strung upon filaments of catgut a number of hollow sections of decalcified rabbit bones, while Segale recommended tubes of ivory or ebony, and Cecherelli and Bionchi plates of whalebone. These ingenious devices are, however, inferior to others which are less complicated and troublesome.

8. The use of permanent forceps or clamps is often of great service.

9. The elastic ligature, especially in pedunculated tumors, has had many adherents. It is generally used extraperitoneally, although not necessarily so. If the pedicle is large the ligature

Fig. 2.



The continuous lines represent a continuous double thread passed backward and forward through the liver by means of a blunt needle, so as to form a series of loops. By dividing the loops, separate ligatures are obtained, which are tied as indicated by the dotted lines. (Terrier and Auvray.)

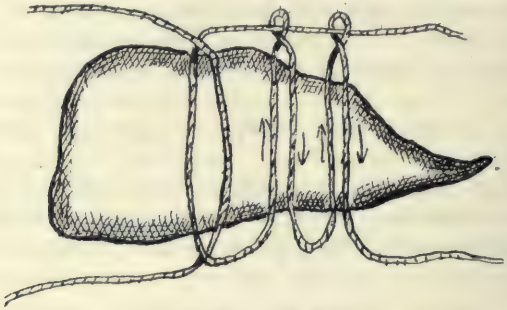
may require tightening from time to time (Lücke), and care must be used to prevent too rapid cutting of the tissues.

10. It has been suggested that bleeding may be checked by stitching omentum over the raw surface. Although this may occasionally be of some service, it can have no extended applicability on account of its unreliability and the amount of time consumed.

11. A method which has attracted much attention was presented by Kurznezow and Pensky in 1886 (Fig. 2), and modified by Auvray in 1897 (Fig. 3). It depends upon the principle that when a ligature is tied tightly about a section of liver, not too large, the parenchyma gives way, but the contained vessels are gathered

into a bundle and held firmly (Fig. 4). The procedure is certainly effective when properly carried out; but it requires time and care, and the somewhat elaborate technique is usually forgotten when needed, which is apt to be unexpectedly.

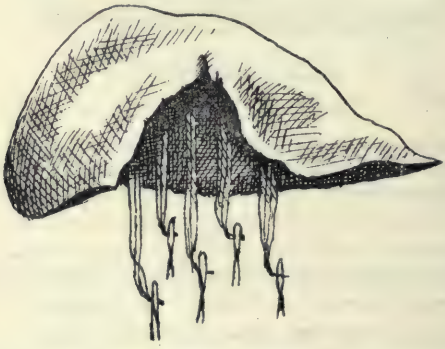
Fig. 3.



Terrier and Auvray.

12. The liver substance surrounding the tumor may be easily ligated with narrow strips of gauze pulled through with long, blunt forceps, as suggested by W. Müller, who treated the stump, however, extraperitoneally. The writer's method of employing these strips intraperitoneally is detailed in the report of his case.

Fig. 4.



Terrier and Auvray.

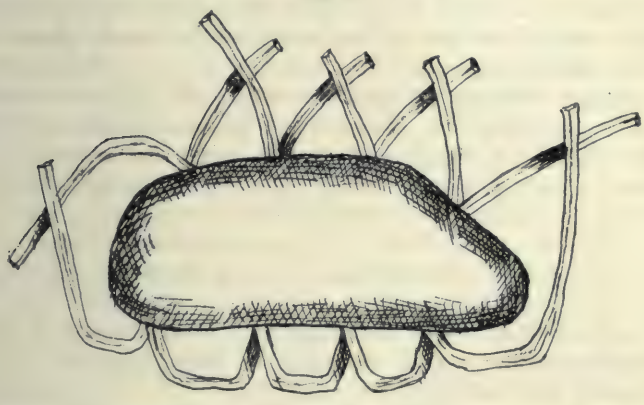
13. In some instances, either alone or in connection with other procedures, the hepatic vessels may be seized with forceps, pulled out from the cut surface, and easily ligated. Experiments have shown that they will stand a traction equal to 750 or even 850 gr.

Report of Case. A well-developed, muscular, locomotive engineer, aged twenty-seven years, had been annoyed for a year

or more by heaviness and moderate pain in the region of the gall-bladder, with occasional exacerbations accompanied by slight jaundice and marked indigestion. Examination revealed a hard, irregular tumor, apparently about the size of a walnut, although the patient stated that it sometimes became larger and more tender. It occupied the position of the gall-bladder and moved up and down with respiration. A diagnosis was made of a gall-bladder tightly filled with stones, although this was done with reservation, because of the mildness of the symptoms in spite of the size, irregularity, and hardness of the tumor.

Operation (*January* 20, 1903). A longitudinal incision through the right rectus revealed a hard, nodular tumor of the left lobe of the liver, just to the left of the notch. It was the size of a large fist, buried almost completely in the substance of the organ, and without

Fig. 5.



a pedicle. The greater part of the growth lay beneath the free hepatic border, so that a small portion only could be felt by abdominal palpation. There were extensive omental adhesions, but no enlarged glands, and the remainder of the liver was free from involvement as far as could be detected. The gall-bladder was normal.

After enlarging the incision it was decided to isolate the tumor by means of ligatures formed from narrow, folded strips of gauze, such as are found in every operating-room. The liver was perforated with long, blunt forceps and the strips pulled through—at first two strips, and then, through each successive hole, an end of the previous strip together with a fresh one. A series of loops were thus obtained, each one enclosing a considerable amount of tissue (Fig. 5). These were slowly and forcibly tightened and tied, thus effectually compressing the liver, but not cutting it as do

ordinary sutures. Hemorrhage from the perforations was prevented by the presence of the gauze.

The tumor was then removed by cutting through normal liver tissue with a scalpel, no bleeding following the section except from a single vessel not included in the ligatures. After sinking the stump in the abdomen it was packed around with gauze, the ends of which, together with the ends of the strips, being brought out through the partially open wound.

The progress of the case was uneventful except in one respect—the removal of the gauze ligatures. The knots being buried deeply in the wound, they could not be untied or even cut with certainty. After some difficulty several strips were finally extracted; but the others resisted all efforts until bands of rubber were attached to them so as to exert constant traction, when they came out promptly and easily and without pain. At another time I should be inclined not to tie the strips, but merely draw them tight and clamp them with forceps, or tie them with catgut, thus admitting of comparatively easy extraction; but in case a strip should stick, elastic traction could still be employed.

The patient left the hospital in about six weeks, completely recovered. On May 18, 1904, about sixteen months after the operation, he was perfectly well, with no signs of recurrence, no disturbance of any kind, and doing regular work on his engine.

PATHOLOGICAL REPORT (DR. J. A. WILDER, OF DENVER).

Gross Appearance. The free surface of the specimen is irregularly nodular in appearance, the nodules being smooth, rounded, and elevated, and merging into each other.

On section the tissue which forms the greater part of the specimen cuts with considerable resistance, being very tough and fibrous, and light in color, in marked contrast to the liver tissue proper. In several places a sharp line of demarcation can be seen between the neoplasm and the liver substance.

Microscopic Examination. Specimens hardened in formalin and alcohol, embedded in celloidin, and stained with the usual stains. Sections were made from blocks taken from the periphery of the neoplasm and from its central part, as well as from blocks including both liver tissue and neoplasm. Sections from the peripheral portion consist of a well-marked stroma of dense connective tissue which forms irregular alveoli in which the cellular material, which is of the glandular epithelial type, is compactly arranged. In some places the cells are so arranged as to give the appearance of atypical and irregular gland tubules, the cells approaching the columnar type and being arranged in several layers. No basement

membrane can be seen. In most fields the alveolar arrangement with the cells completely filling the spaces is most conspicuous. In some places the cells are arranged in long columns which are surrounded by the connective tissue. The cells are large and have large round or spheroidal nuclei that take the stain with moderate intensity and contain distinct nucleoli. The cytoplasm is present in considerable amount, its periphery in some of the cells being distinctly outlined, but in the majority indistinctly, the cell bodies appearing to have coalesced.

The majority of the cells that can be accurately measured are from 16 microns to 22 microns in diameter, their nuclei measuring from 7 to 12 microns. Sections from the blocks in which both liver tissue and neoplasm were included show a broad band of connective tissue between the two, which has been infiltrated in various places by the tumor cells. The liver cells differ very materially from those of the neoplasm in general appearance, staining reaction, arrangement, and regularity. They show a moderate amount of parenchymatous degeneration. The stroma is abundant and consists chiefly of adult fibres of connective tissue, giving the picture of scirrhus in many places. In some parts the stroma is infiltrated by collections of lymphoid cells. The vascular supply is rather poor, but a few vessels with well-developed walls are present in the connective tissue. The stroma contains also a few apparently normal bile-ducts. An effort at encapsulation by dense connective tissue appears to have been made at the periphery of the nodules, but this tissue had been infiltrated in many places by the epithelial cells. The distinctly adenomatous appearance of the growth in some places and the characteristics of the epithelium present are suggestive of the possible origin of the neoplasm from the bile-ducts.

Histological Diagnosis. Adenocarcinoma.

THE SHAPE OF THE CHEST IN HEALTH AND IN PULMONARY TUBERCULOSIS.

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and

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Introduction. Since the time of Hippocrates the shape of the human chest and its changes in disease have been often discussed. On account of the widespread prevalence of pulmonary tubercu-

losis the attention of many observers in all ages has been drawn to the disease, and much has been written about the shape of the chest in pulmonary tuberculosis. Hippocrates described a type of chest in pulmonary tuberculosis which is smaller than the normal chest, but has the same general outline. The scapulæ do not lie flat on the posterior wall, and this projection has given the name alar to this type of chest. Galen has added that the chest is narrow and shallow, and Gee[1] states that the anteroposterior diameter is especially small, "but the diminution in capacity presented by the alar chest does not necessitate any great change in the outline which a horizontal plane of the thorax naturally presents." Dr. Gee then describes a second form of chest frequently occurring in pulmonary tuberculosis, the flat chest, which has its anteroposterior diameter lessened. These views have been generally accepted (Osler,[2] Musser,[3] Fraenkel,[4] Steel,[5] etc.) without further investigation, and where any authority is mentioned reference is generally made to Gee.

In 1897 Dr. Woods Hutchinson called in question these generally accepted views and stated that the flat chest of phthisis was only apparent, not real. A series of measurements was instituted at the Adirondack Cottage Sanitarium in 1901, with a view to throwing additional light on the question. It was thought too that any physical characteristic should be reduced to a basis of measurements, and entire reliance should not be placed on the judgment of the eye.

Hutchinson's Theory. In the *Journal of the American Medical Association*, September 11, 1897, Dr. Hutchinson first published the result of his chest measurements. He further elaborated his views in his book (*Studies in Human and Comparative Pathology*), and again in 1903 (May 2) wrote in the *Journal of the American Medical Association* an article, "Is the Consumptive Chest Flat?" He compares all chests by means of the "chest index," which is defined as the ratio of the anteroposterior diameter to the transverse diameter. He takes for his normal type the results obtained from the Yale anthropometric table compiled from the measures of 2300 students by Dr. Jay W. Seaver and 50 measurements made by himself on soldiers at Fort Porter. His tuberculous type is based on measures from 350 cases, mainly from various hospitals (Brompton, etc.) and in advanced stages of the disease, collected by various medical men as well as by himself.

He concludes from these measures that:

"1. The typical tuberculous chest is round instead of flat and has an average index of about 80, nearly ten degrees above the normal (70).

"2. This type of chest precedes the disease.

"3. It is an abnormal persistence of the fetal, infantile, and child type of chest.

"4. Any chest more than eighteen years of age that shows an index of 80 or higher should be regarded as abnormal and as rendering its possessor more than usually liable to tuberculosis.

"5. The occurrence of such a chest in any person over eighteen years of age suspected of tuberculosis raises a strong probability of the disease.

"6. The chests of growing boys and girls should be systematically measured at stated intervals, and whenever the index is found distinctly higher than the normal for their age active measures should be taken to remedy the defect.

"7. All those sports and exercises which involve wide-swinging use and play of the arm, chest, shoulder group of muscles, such as tree climbing, swinging from ladders, from rings, from bars, ball throwing, spear hurling, tennis, swimming, will tend to correct this defect and flatten the chest down to its proper index."

The Index of the Normal Chest. In order to discuss any variation, it is of the utmost importance to settle definitely if possible upon a normal. Almost at the beginning of this inquiry it was felt that before conclusions could be safely drawn it was necessary to have further data in regard to the normal adult chest. Information as to the absolute measures at various ages, the effect of age and development on the index after childhood, the range of index in normal individuals, etc., were of fundamental importance. That the average index of the soldiers who were older men and under special physical training was higher than that of the Yale students seemed worthy of attention. A comparison of chest measures in patients emaciated from causes other than pulmonary disease seemed also desirable. The question of the female chest, which Dr. Hutchinson thought had normally a higher index than the male, had also to be investigated. After searching in various directions with very little result, Dr. D. A. Sargent, of the Hemenway Gymnasium, at Harvard, kindly offered to take a series of measurements, and later forwarded the measures of 540 males and 180 females. An anthropometric table, compiled by Annie L. Barr, Director of the Women's Gymnasium, University of Nebraska, was also obtained. Certain measurements quoted by Musser and Gee, notably those of Otis, of Boston, have been used. Dr. Stroud, of Tufts College, has been so kind as to send measurements of 102 of his college students. The anthropometric table of 2300 Yale students, compiled by Dr. Seaver, has also been used in estimating the normal.

The Yale table, from which Dr. Hutchinson draws his normal, differs markedly from the other sources of information. The 50 soldiers which he measured at Fort Porter give an index of 73.9, and two other short series (where numbers are not stated) give 71.5 and 72.6, respectively. While the individual measures for the Yale cases are not obtainable, yet it is highly probable that the average index would not differ materially from the index obtained by using

the normal diameters (69.3). The measures of 540 Harvard students (males) indicate an average index of 77.5. In a series of measures taken by Dr. E. O. Otis, 1250 of the depth of the chest and 400 of the breadth of the chest, the index resulting from the averages was 75.8, agreeing very closely with Dr. Sargent's. Several measurements given by Gee would indicate a normal index of 74 or 75. Dr. Stroud's measures taken at Tufts College have an average index of 68.2.

Taking the series of fetal, infantile, and child indices as given by Dr. Hutchinson, it is found that the change during the first few years is large, but rapidly decreases as age advances. This fact has long been recognized. If a curve is plotted, it is found that, taking Dr. Sargent's or Dr. Otis' figures at the mean age (about twenty years), the indices of 77 and 76 form a consistent continuation, but the index from Dr. Seaver's Yale measurements cause a sharp bend in the curve. However, combining the Yale, Harvard, Otis, and Fort Porter measures, a normal index of 73.2 is obtained.

The index of the normal female chest is stated by Dr. Hutchinson to be higher than that of the male. The average index of the female student at the University of Nebraska from Miss Barr's measures is 67.7. From 180 female cases measured by Dr. Sargent, the average index was 70. From this it seems that the female chest index is lower than the male—*i. e.*, the female chest is flatter than the male.

Method of Taking Measurements. After the collection of these various data it was found that the measures were not all taken under exactly the same conditions, and that allowance would have to be made for this. Hutchinson's measurements were made at the level of the nipples or of the middle of the fourth intercostal space at the post-expiratory pause. Sargent's were made at the level of the nipples after a natural inspiration, and Seaver's at the same level "in ordinary quiet position without forced inspiration," while Otis recorded his presumably at the same level at repose and on inflation. To estimate what allowance should be made for the variations caused by these differences in obtaining the measurements, 25 cases at the Adirondack Cottage Sanitarium were measured. It is fully recognized that the respiratory movements in these cases may be slightly less than in the healthy, but still some guidance can be obtained from them. The average difference in the anteroposterior diameters taken after quiet inspiration and expiration was 0.42 cm., that of the transverse 0.52 cm., amounting in each case to about 2 per cent. of the absolute measures. It was early recognized that the level of the nipples varied considerably, and it was thought better to select some bony prominence as a guide. Hutchinson used, in some cases, the middle of the fourth interspace, but on account of confusion in estimating this point (Hutchinson did not state whether he took the level at the sternal border or in the nipple line), it was

thought better to select the level of the fourth costal cartilage. To determine what variations might occur from measurements taken at these different points, 25 cases at the Adirondack Cottage Sanitarium were measured. Measurements of the anteroposterior and transverse diameters were taken at the level of the juncture of the fourth costal cartilage and the sternum and at the level of the nipples. It was found that these two levels varied considerably, depending upon the obliquity of the costal cartilages and the ribs. The difference in level ranged from 1.5 to 5.5 cm., and averaged 3.4 cm. The transverse diameter varied very little, the average difference, an increase at the nipple level, being less than 1 per cent. (0.8 per cent.). The anteroposterior diameter, however, varied considerably over 3 per cent. (3.6 per cent.), being deeper at the nipple level. This change in relative measurements caused a change in the index of about 3 per cent., or two degrees—*i. e.*, from 69.4 at the level of the fourth costal cartilage to 71.4 at the level of the nipples. From these observations, especially from the difficulty in obtaining the transverse diameter at the level of the fourth costal cartilage, it is best to select the junction of the fifth costal cartilage with the sternum as the level on which to take the diameters of the chest. The post-expiratory pause seems to be the best time in which to take the measurements.

This experience brings into prominence the desirability of greater uniformity in the method of taking anthropometrical measures, so that the data collected by different observers may be compared or combined, and so that the collectors of any such measures in the future may know what is the best method of procedure.

Statistical Methods. In any investigation depending largely on the analysis and comparison of series of measurements, the choice of the statistical methods to be employed is of great importance. The use of the average or arithmetical mean to represent a series oftens leads to serious error, and is only appropriate under certain well-defined conditions:

1. The series must be homogeneous in regard to any characteristics which might affect the result. A familiar illustration of error arising from neglect of this condition is furnished by a comparison of the general death rates of two cities in which the age distribution of the population is very different. While the death rates for each age may be the same in both places, yet the general total death rates may vary widely, owing to the population of one city consisting mainly of those in the prime of life, while the other contains a much larger population of children and aged persons, among whom the mortality is much higher.

2. Variations from the normal must be, *a priori*, equally probable in either direction; in other words, the law of variation must be the binomial or exponental law. Many of the measurements of the human body do not fulfil this condition, as has been repeatedly

pointed out. Further evidence of this is furnished in the study of the chest measurements, which follow. Even when both the foregoing conditions are fulfilled, the average may not satisfactorily represent the tendency of the series, and is by itself of little value for making comparisons, as it in no way indicates the degree of divergence from the mean, which is in general one of the most important characteristics of a group of measurements.

Of the two most fruitful methods, one consists in arranging the measures forming the series in the order of their respective magnitudes, showing the number of cases at each magnitude or in the interval between a set of equidistant magnitudes. The magnitude or interval under which the greatest number of cases occurs is then taken as the normal. When the above results are plotted on squared paper, the magnitudes or intervals being the abscissæ, and the numbers of cases the ordinates, the resulting curve gives a graphic representation of the series in a very convenient and suggestive form. When a series is homogeneous and not subject to any influence rendering variation in one direction more probable than in the other, a symmetrical curve approximating to the type of the probability curve is obtained. Any variation from this type demands careful consideration. When a series is small and gives a very irregular curve, it is often advantageous to group several consecutive magnitudes together, and thus secure a more regular progression, taking care, however, that in so doing no essential characteristic of the series is lost. The other method referred to is that due to Galton, and is known as the percentile method. This consists in arranging all the measures in the order of their magnitude and taking the central value as the normal, arranging the other values in accordance with the percentage of the total cases which exceed or fall short of them.

The degree of confidence which obtained results should warrant is often hard to determine. In general the weight of an average is proportional to the square root of the number of measures of which it is the mean—*e. g.*, a series of 400 cases has only twice the value of a series of 100. When, however, several independent series give the same result, the reliance warranted is greater than that called for by the same total number of cases all belonging to one series. The average gives sometimes undue weight to a few abnormal cases and to errors, and the other two methods are far superior in this respect. The "frequency" method is generally preferable where it is desired to present the results of a series in a form giving the greatest amount of information in the smallest space. When the frequencies are given, the average and percentiles can easily be calculated; where only the average is given, even with a statement of the average deviation or error, neither the frequencies nor the percentiles can be gotten; and where the percentiles only are given the calculation of the average and the frequencies is not possible. The

graphical method of presenting the frequencies is, perhaps, the most satisfactory way of all. "When there is some degree of asymmetry," writes Prof. Venn, of Cambridge, "it is the maximum ordinate which would have to be considered as a mean to the exclusion of the others, for no appeal to an arithmetical average would guide us to this point, which, however, is to be regarded, if any can be so regarded, as marking out the position of the ultimate type."*

THE EFFECT OF AGE, GROWTH, AND DEVELOPMENT ON THE SHAPE OF THE CHEST. After growth in height has practically ceased, the development of the body in other ways still continues. The data for discussing this question are, however, very few. The Adirondack Cottage Sanitarium cases being underdeveloped and diseased, cannot be used as a certain guide, and the measurements of college men and women are very few beyond twenty-two years of age. The 50 measurements of soldiers collected by Dr. Hutchinson commence at twenty-one, and, to a certain extent, supply the want, though, as these men are constantly undergoing special training, too much weight cannot be given to inferences derived from them. However, taking all the series together, it seems safe to conclude that development in both diameters of the chest continues much longer than increase in total height.

The increases in the diameters from birth to manhood are, as stated before, not proportionate, the transverse increasing more rapidly than the anteroposterior diameter. This tendency of a decrease of index appears to continue up to a certain period (eighteen to twenty-four years), and then a change occurs, resulting in a tendency of an increase of the index. The definite cause of this increase of index has not been determined. Gee has noted that in advanced years there is some tendency for the chest to revert to the configuration of childhood. In every series of measurements available this tendency is shown. The Harvard measurements show the early decrease and later increase of the chest index with age (sixteen to eighteen years, index 78.3; nineteen years, 76.3; twenty years, 77.3; twenty-one years, 76.6; twenty-three years and over, 79.6). While in the tuberculous cases no doubt other factors may occur, still the tendency is very striking.

COMPARISONS OF VARIOUS SERIES OF MEASURES. The various series of measurements have been represented graphically and some shown in the accompanying diagrams, but each measurement is considered separately. It has been thought best to treat separately the measurements obtained in cases of pulmonary tuberculosis from those obtained in normal chests.

Table I. shows the average (absolute) changes in the various measures concurrent with age and development. The tuberculous cases follow the same law.

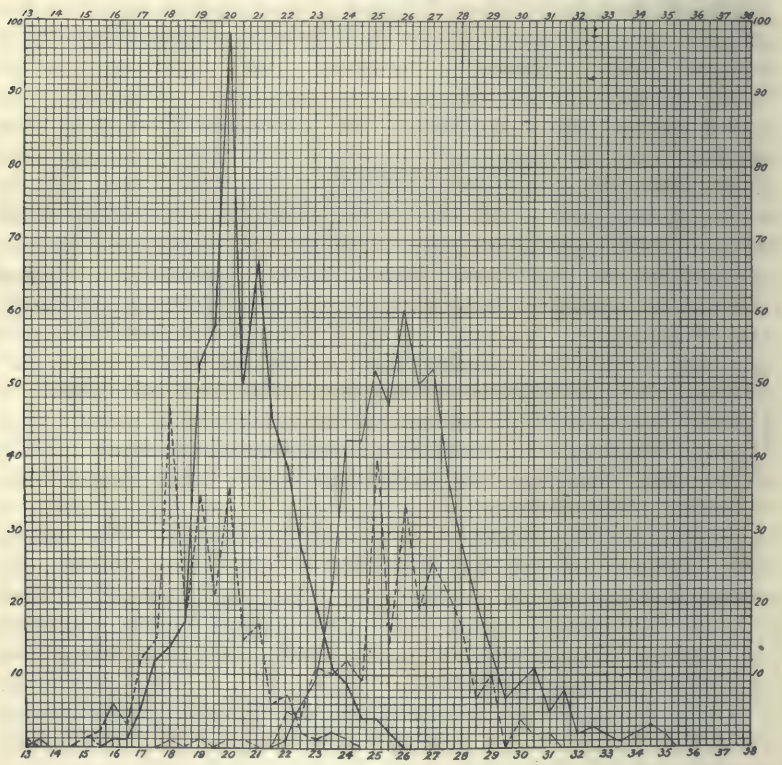
* Logic of Chance, p. 455.

TABLE I.—Variation of chest measurements for age and sex.

Sex.	Ages.	Cases.	Antero-posterior diameter.	Trans-verse diameter.	Index.	Length.
Male	16–17–18	131	20.16	25.77	78.3	33.14
"	19	113	20.40	26.77	76.3	32.96
"	20	104	20.87	26.75	77.3	33.25
"	21–22	117	20.60	26.67	76.6	33.21
"	23 & over	75	20.93	26.45	79.6	34.05
Female	16–17	34	17.45	24.72	70.6	29.98
"	18	73	17.57	24.95	68.0	30.51
"	19	49	17.81	24.66	72.2	31.47
"	20 & over	24	17.79	25.10	71.1	31.59

THE SHAPE OF THE CHEST IN HEALTH. *The Anteroposterior Diameter in Males.* The Fort Porter maximum is most marked at 20.5 cm.,* the Harvard at 20 cm.,† and the Tufts at 18 cm. (See Chart I.)

CHART I.



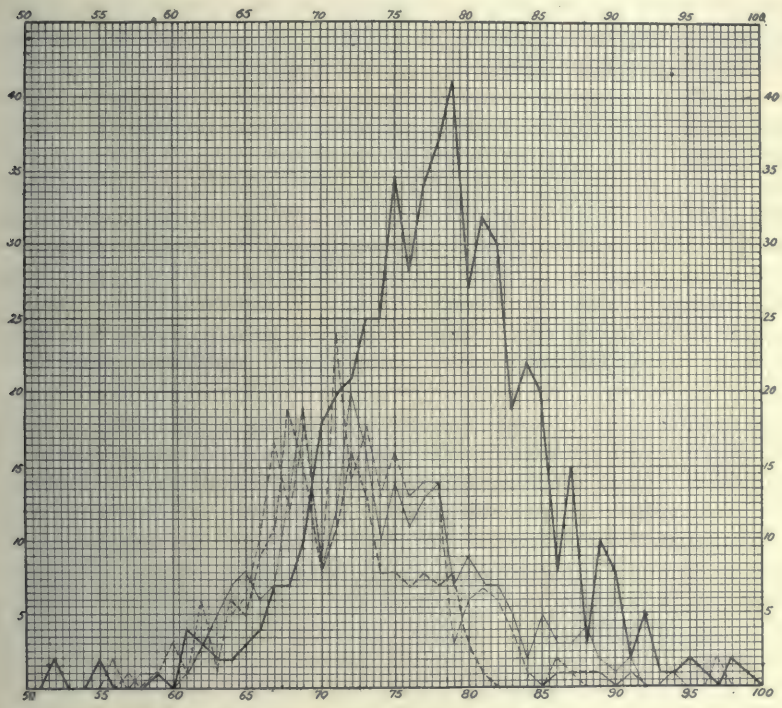
* The Fort Porter cases were measured by Dr. Woods Hutchinson.

† It should be recalled that the Harvard measures are taken at the post-inspiratory and not post-expiratory pause, causing a difference of about half a centimetre.

The Transverse Diameter in Males. The Tufts maximum is 28 cm.; the Harvard, 26 cm.; the Fort Porter, 26.5 cm.; and the Yale mean is 27 cm. The Fort Porter cases show a tendency toward a submaximum at 28.5 cm. In each series there is a less strongly marked normal transverse diameter than in the case of the normal anteroposterior diameter. This would in all probability indicate that there is in general a greater variation in the transverse diameter than in the anteroposterior. (See Chart I.)

Chest Index in Males. The variations in the frequency of the chest index average is striking: Harvard, 79; Fort Porter, 73; and Tufts, 66 and 69. (See Chart II.) The ratio of the means at Yale is 69.

CHART II.



The Length of the Chest in Males. The length of the chest has a comparatively wide range, between 33 and 36 cm., and no well-defined maximum.

The Anteroposterior and Transverse Diameter in the Female. For the anteroposterior diameter the Sargent measures have a maximum at 17 cm. For the transverse diameter the Sargent maximum is at 24.5 cm.

The Chest Index in the Female. The tendency of the chest index seems to be lower than in the case of males. (See Chart II.) The

Sargent cases have a maximum at 68. The ratio of the means of the University of Nebraska is 68.

Length of the Chest in Females. The Sargent data show that the range of length is about 3 cm. less than in the male.

THE SHAPE OF THE CHEST IN PULMONARY TUBERCULOSIS. Few measurements of the chest in pulmonary tuberculosis taken previous to this time have been found of value for this study, as they do not include the diameters. It is well always to bear in mind that individuals with apparently normally shaped chests may be liable to pulmonary tuberculosis—*i. e.*, chest configuration renders no one immune. "My examination of some 6000 nude chests," says Alison,[6] "at the Consumption Hospital (Brompton) has established several facts in connection with this subject. The first is this: Comparatively few greatly distorted chests are seen among phthisical patients; I believe not more in proportion than are found in persons not suffering from phthisis. I have met the greatly distorted chest, the greatly gibbous back and sternum of rachitis in not more than some six persons suffering at the same time from decided phthisis; while among this number of 6000 I have seen this distorted chest in at least some dozen suffering from dyspnœa and bronchitis.* The finest specimens of the human thorax I have constantly seen associated with tubercular disease of the lung, and I believe that persons having this development are not materially less liable to phthisis than others." The experience at the Adirondack Cottage Sanitarium fully confirms this. Alison, however, goes on to say that the flat chest, which has been held to predispose to pulmonary tuberculosis, is the consequence of it, and the departure from the healthy or normal form may prove, especially where the acoustic signs are deficient, "an aid of some value and deserving of some reliance." In other words, careful inspection of the chest in pulmonary disease is of great value in many early cases.

Adirondack Cottage Sanitarium Data. Chest measurements have been taken at the Adirondack Cottage Sanitarium on and off for a number of years, but until February, 1901, the measurements were not taken in sufficient detail and exactness to be of much value. From time to time measurements of various parts have been added, until at present the following measurements are taken in all cases on admission and discharge (height on admission only): Height, girth of chest at level of the fourth† costal cartilage on quiet breathing, forced inspiration and forced expiration, length of chest, diameters of chest in a horizontal plane during post-expiratory pause (anteroposterior diameter, sternum to tip of spinous process; transverse diameter, over ribs, not in interspaces) at the level of the fourth

* This was written before the discovery of the tubercle bacilli.

† Since these measurements were taken the level of the juncture of the fifth costal cartilage and sternum is used.

costal cartilage and at the tip of the ensiform cartilage; the anteroposterior diameter at the top of the sternum, breadth of nipples, diagonal diameter in a horizontal plane from the vertebral spine to the right and left nipples.

In this investigation the diameters at the level of the fourth costal cartilage, the length of the chest in the midclavicular line parallel to the midline and the expansion (the difference at the fourth costal cartilage between the girth on quiet and forced inspiration), and the respiratory movement (the difference at the same level between forced expiration and forced inspiration) are the only measures considered. In considering change in the shape of the chest the diameters afford a means of comparison more accurate than the circumferences, on account of the increase of adipose tissue. It may be added that the patients at the Adirondack Cottage Sanitarium are drawn from all classes of society, from varied races, and from all parts of the continent, so that they are fairly representative of the general public and not merely of a class or section.

The Diameters, Length, and Index of the Chest in Males. The maximum of the anteroposterior diameter of the Adirondack Cottage Sanitarium cases is most marked at 18 cm. (See Chart I.) The normal anteroposterior diameter may be stated to be about 20.5 cm. When divided into stages the maximum of the cases at the Adirondack Cottage Sanitarium are:

Incipient	19 to 20 cm.
Advanced	18 cm.
Far advanced	18 cm.

The advanced cases have a marked submaximum at 20 cm.

The transverse diameters show a maximum at 25 cm. in the Adirondack Cottage Sanitarium cases, and at 24 cm. in the Brompton cases. The Adirondack Cottage Sanitarium cases treated as before give:

Incipient	27 cm.
Advanced	25 cm.
Far advanced	No definite maximum.

The normal transverse diameter is about 28 cm.

The normal chest index may be said to range between 72 and 75. The index of the Brompton cases was 80, that of the Adirondack Cottage Sanitarium cases 72. (See Chart II.) On separating the Adirondack Cottage Sanitarium cases as before, we get:

Incipient	69 and 72 cm.
Advanced	68 and 71 cm.
Far advanced	No definite maximum.

The far-advanced cases show a tendency to have a higher index than the others.

The length of the chest in the Adirondack Cottage Sanitarium cases seems slightly larger than that in the Harvard cases, while the Fort Porter and Brompton cases are much shorter. The incipient cases among the Adirondack Cottage Sanitarium cases seem slightly longer than the advanced. When compared with the height of the patient, more striking results are obtained. Fifty per cent. of the Harvard cases show a ratio of 19.1. The same proportion of the Adirondack Cottage Sanitarium cases show 19.9, and this in spite of the fact that the heights in the latter are inclusive of shoes, which seems to confirm the view that the consumptive chest is long relatively to the height of the person. The Brompton cases and those at the Adirondack Cottage Sanitarium who are far advanced show a much shorter chest.

The Chest in Females. The maximum for the anteroposterior diameter in females at the Adirondack Cottage Sanitarium was 18 cm., 1 cm. longer than the Sargent cases. This difference is probably largely due to age, as the Sargent group of cases are comparatively young. The transverse diameter, however, shows a maximum for the Adirondack Cottage Sanitarium cases at 24 cm., and Sargent's at 24.5 cm. The general tendency for both measures is for those of the Adirondack Cottage Sanitarium to be smaller than the Sargent cases, and this in spite of the difference in age. The incipient group shows a slight tendency to be a little smaller in both diameters.

There is no definite preponderance of any index type in the Adirondack Cottage Sanitarium cases, where the maximum is about 71.3 degrees higher than the index of the Sargent cases. (See Chart II.) The incipient cases have a maximum at 71, the advanced at 69, the far advanced at 71 to 74.

Nothing can be said in regard to the length of the chest in females, as there are too few measures upon which to base any conclusions.

Effects of Emaciation. To determine the effect of emaciation and consequent loss of musculature, a series of measures were taken in a number of emaciated cases whose lungs and heart were apparently normal. The number of cases found fulfilling these conditions were small, and the results are, therefore, inconclusive; but the facts obtained point to the conclusion that much change of index is not necessarily associated with emaciation. Eleven male cases had an average index of 71, 7 females of 73.4.

Changes in the Shape of the Chest during Sanitarium Residence. When considering the changes in the shape of the chest during Sanitarium residence various factors have to be taken into account. The average Sanitarium residence is about seven months, and during this period many patients undergo a marked change in health and general condition. A summary of the changes in measures between admission and discharge furnishes interesting results. (See Table II.)

TABLE II.—Changes in chest measurements during Sanitarium residence.

Sex.	Condition.	Anteroposterior diameter.			Transverse diameter.			Length.		
		Admission.	Discharge.	% increase.	Admission.	Discharge.	% increase.	Admission.	Discharge.	% change.
Male	Incipient	19.20	19.79	3.0	26.36	27.16	3.0	34.37	34.07	—0.9
"	Advanc'd	18.92	19.35	2.0	26.17	26.79	2.4	34.64	34.68	+0.1
Female	Incipient	16.86	17.25	2.0	23.61	24.01	1.7	33.54	33.34	—0.3
"	Advanc'd	16.96	17.47	3.0	23.69	24.58	3.8	33.94	34.04	+0.3

Both diameters of the chest show a clearly marked increase of 2 to 3 per cent., which is far in excess of what could be accounted for by the slight increase in age. These increases when considered as a whole show a tendency to be proportional to the diameters and do not alter the average index appreciably. The possibilities of the transverse diameter as to development appear to be much greater than those of the anteroposterior. If the cases showing an increase of index are grouped together and those showing a decrease, the averages of the two are markedly different. Moreover, when the cases are separated into several groups according to the index on admission, those groups with a low average index on admission show an increased index on discharge, while those with a high index on admission show a decreased index on discharge. So it appears that there is a reduction of the extreme indices at both ends of the scale (below 69 and above 80) and also a reduction in the number at the middle (about 72). There is a further tendency to gather around two index points, about 69 and 80, which appear possibly to represent two types of chest. From measures taken on admission and discharge in 130 males and 134 female patients, slightly more than 10 per cent. show changes of index of 5 degrees or more. Changes of 3 and 4 degrees are frequent. From this it would appear that the shape of the chest is easily modified within certain limits, and this conclusion is strengthened by the fact that the vast majority of cases show some change in the index. Further, it would seem that whatever the cause may be there is a very wide range to the index possibilities of the normal chest, from say 60 to 85. The elevation of 1600 feet has not been considered sufficient to produce much change from the rarefaction of the atmosphere.

The ratios of the chest diameters to the height of the individual are less in advanced than in incipient cases, and less again in the far advanced. The progress of the disease seems, therefore, to affect the diameters.

The most striking change is the increase in the expansion and respiratory movement. For comparison with Table III. the following figures are of value: Expansion (in millimetres) male: Yale,

49; Amherst, 48; Williston, 47; Cornell, 45.7. Female: Nebraska, 59; Mt. Holyoke, 48. Respiratory movement: Mt. Holyoke, 95.

TABLE III.—Changes in chest measurements during Sanitarium residence.

Sex.	Condition.	Expansion.				Respiratory movement.			
		Admission.	Discharge.	Difference.	% increase.	Admission.	Discharge.	Difference.	% increase.
Male	Incipient	4.46	4.84	0.38	8.6	8.92	10.38	1.46	16.1
"	Advanced	4.17	4.63	0.46	11.1	7.80	9.85	2.05	26.3
	Total	4.26	4.70	0.44	10.3	8.18	10.03	1.85	22.1
Female	Incipient	3.40	3.56	0.16	4 7	7.51	8.51	1.00	13.3
"	Advanced	2.96	3.25	0.29	9.9	6.34	8.41	2.07	32.7
	Total	3.12	3.36	0.24	7.9	6.73	8.44	1.71	25.5

Predisposition to Pulmonary Tuberculosis and Chest Index. To determine whether any particular chest index is especially subject to tuberculosis, two courses are open, both of which should give the same results. The first is to take the measures of a number of young people and see how they turn out in the course of say ten or fifteen years. This is almost impossible, and is subject, unless the number of cases is very large, to many sources of error, owing to the varying environments of the individuals.

The second method is to take a series of cases in the early stages of tuberculosis before the disease has had much opportunity to affect the shape of the chest (an important factor which acts more rapidly than is often supposed) and to compare them with a series of healthy individuals to see whether there is any difference in the proportion of cases at any of the indices. If a considerable difference is found in the frequency curves of the two series it may reasonably be concluded that there is some causal connection between index and disease, but, on the other hand, when the curves are practically identical, then it can as surely be considered that the shape as distinguished from the size is not a causative factor in the case. Comparisons of the frequency curves would seem to show slightly opposite results in the males and females; but, on the whole, the conclusion appears warranted that no one index of the chest can at present be said to be more liable to consumption than others.

In conclusion, it may be said that in attempting to formulate a standard for the dimensions of the chest it must be borne in mind that there is no absolute standard of human development. Each race has its own peculiarities, and in each race there is a wide range of divergence. It is about impossible to determine the normal type, as so many influences affect it. What is normal for one class is

extremely abnormal for another. This applies not only to the measurements themselves, but also to their relations to each other. Results in mass tend to gather around some central value which there is a great temptation to regard as a type, an end at which nature was aiming, but when further analysis is made, this value is found to vary from class to class and to have no existence in itself, but to be merely the result of the combination of several different series. For instance, the mean British stature of 67.66 inches splits up into English, 67.36; Scotch, 68.71; Welsh, 66.66; Irish, 67.90. These again could be subdivided into various classes with still further varying results. This seems to be especially true in any discussion of the chest index.

Comparison by the "Average" Method. The method of comparison in this article, which may be termed the "frequency method," yields, it is believed, as has been stated before, more accurate results than the method of "averages." However, it has been deemed expedient to give here the results obtained by the latter method. Table IV. gives the averages for each measure, the chest index, and the ratios of the anteroposterior and transverse diameters to the height of the patient. The smallness of the diameters in the Adirondack Cottage Sanitarium cases is real and not merely a consequence of the patients being small generally, as is shown by the ratios of depth and breadth of chest to total height of person, especially when allowance is made for the underdevelopment of the majority of the college men on account of their youth. Combining the Yale, Harvard, Fort Porter, Tufts, and Otis measurements in the male, the average anteroposterior diameter for the healthy chest is 19.1 cm., the average transverse diameter 26.7 cm., and the average index 71.4. For the consumptive chest the figures are 19.3 and 25.9 cm. and the index 74.6. For the female the normal figures are 17.64 and 24.85 cm., and 70.0; the consumptive, 17.1 and 23.7 cm., and 72.6. It must not be overlooked, however, that a greater part of the healthy chests included in these averages are young and not fully developed. This makes the average diameters less than the adult normal. The Yale cases, further, are more than two-thirds of the total, so that they have a preponderating influence on the results. That the difference between the average index of Dr. Hutchinson's consumptive cases and the Adirondack Cottage Sanitarium cases is so much greater than between the Adirondack Cottage Sanitarium and the average of all healthy cases obtained would seem strong evidence that the high index is a result and not a precedent of tuberculosis.

While studying the ratio of the chest diameter to the height by ages it was clearly shown that there is at first a marked decrease and later a marked increase of the ratios.

Relation of Race and Index. No definite relation seemed to exist between race and chest index in the data at the Adirondack Cottage Sanitarium, but the statistics on this are imperfect and admit of no

definite conclusions. On account of the influence of race on other measures of the body, it is probable that the chest index does not escape this influence.

TABLE IV.—Average of various series of chest measurements.

Sex.	Source.	Cases.	Antero-posterior diameter.	Antero-posterior ratio.	Trans-verse diameter.	Trans-verse ratio.	Index.	Length.
Male	Harvard	540	20.57	11.75	26.46	15.09	77.5	33.30
"	Yale	2300	18.70	10.84	27.00	15.66	69.3	
"	Tufts	102	18.50	.....	27.17	.....	68.2	
"	Otis	400	19.00	.....	25.10	.....	75.7	
"	Fort Porter	50	20.68	12.06	27.97	16.26	73.9	31.91
"	Brompton	40	20.32	.....	25.65	.....	79.6	31.50
"	Adirondack Cottage Sanitarium	249	19.08	11.04	25.93	15.22	73.8	34.28
Female	Sargent	180	17.64	10.89	24.85	15.13	70.0	30.00
"	Nebraska	....	17.00	10.62	25.10	15.69	67.7	
"	Adirondack Cottage Sanitarium	251	17.13	10.51	23.66	14.46	72.7	

Variation in Diameters and Index. The amount of variation in absolute measure required to produce marked changes in the chest index is small. One-half centimetre difference in the anteroposterior diameter makes about two degrees difference in the index, and a half centimetre in the transverse about one and one-half degrees. So a slight difference in both diameters makes a marked difference in the index. For future reference, it may be said that the anteroposterior diameter at the top of the sternum showed a maximum at 14 cm. and averaged 14.35 cm. At the level of the ensiform cartilage the anteroposterior diameter showed a maximum at 19 cm. and averaged 19.34 cm. For the transverse diameter at this level the figures were 26.5 and 26.39 cm.

Heredity and Index. To determine the effect of heredity upon the index, the cases with a tuberculous father or mother, or father and mother, 80 in number, have been studied separately. The cases are too few to base any definite conclusions upon, but the average index for the group was: male, 75.2; female, 72.4. The cases in which the mother alone was affected seemed to have a slightly higher index (75.5) than the average in the male patients, slightly lower (72.4) in the females. The figures vary so slightly from the normal average that no conclusion seems warranted.

Occupation and Index. The relation of occupation and chest index is of interest. The following are the indices for various occupations:

MALE.

Students	(19)	70.05
Clerks, etc.	(44)	72.07
Mercantile and trading	(25)	74.00
Manufacturing and mechanical	(25)	75.32
Farmers and outdoor workers	(18)	76.06
Professional classes	(25)	76.72

FEMALE.

Teachers	(27)	70.59
Manufacturing	(15)	72.60
Housework	(52)	73.11
Trained nurses	(23)	73.52

The lower index of the students and teachers may be partly explained by age. No explanation for the variation of index has suggested itself.

Many minor variations in the shape of the chest in pulmonary tuberculosis have been pointed out. Alison,[6] in 1861, showed that the sternum was flat, and Rothchild[7] has recently called attention to the fact that the Angulus Ludovici is less prominent than usual, and may, in fact, be obliterated. He, as well as Gee, has been unable to find any reference to this angle in Louis' writings, which upholds Conradi's contention that it is well marked in phthisis. He says at the junction of the manubrium and the gladiolus the second costal cartilage is often enlarged, forming a pyriform exostosis, suggesting an apparent increase in the angle. Mensuration proves that, as said before, it is decreased or obliterated and movement at the junction limited.

Freund[8] has stated that premature ossification of the first costal cartilage causes a diminution in the upper aperture of the chest.

Von Behring[9] has recently suggested that many children very early in life may have tuberculosis at the junction of the costal cartilages and the sternum, which may result in some deformity. No observations are adduced to uphold this theory.

While much attention has been given to the shape and the size of the bony structures of the thorax, the size of the lungs has received little or none. There is no inherent reason why an individual should not have a congenitally small or weak pair of lungs. What is true of the heart is probably true of the lungs. The shape of the bony thorax is easily changed within certain limits, and why the atmospheric pressure combined with a congenitally small lung volume should not cause a change in the shape of the chest is difficult to see. This, too, would seem to be a reason why the chest should not be rounder or deeper than normal, although a circumference in the form of a circle includes more space than in any other shape.

CONCLUSIONS. 1. The measurements of the normal chest up to this time have not been determined with sufficient accuracy to allow of very positive conclusions.

2. The influence of race, age, occupation, and altitude must be considered in determining the normal measures and relations. The chief impression gained from this study is that the chest, which is subnormal in its diameters and normal or supernormal in its length, is the chest more subject to pulmonary tuberculosis, though whether in many cases the disease liability and the shape of the chest are not both results of the same conditions and not casually connected, is an open question. Influences which tend to improve the develop-

ment of the chest tend also to prevent consumption, and this may account for the relative immunity of the well-developed chests.

3. The anteroposterior diameter in health may be stated to be about 20.5 cm. at the level of the nipples; the transverse about 28 cm., giving an index of 73. In the early stages of pulmonary tuberculosis the anteroposterior diameter at the level of the fourth costal cartilage is about 19.5 cm., the transverse about 27 cm., giving an index of 72. In advanced stages the figures are about 19 cm. and 25 cm., and index 76.

4. The female chest shows a tendency to a lower index than the male.

5. The chest index is readily changed within certain limits in the individual.

6. The influence of pulmonary tuberculosis has some tendency to reduce the diameters of the chest, and it seems as if it also reduced the length.

7. The progress of the disease probably tends to increase the index, though further data are necessary before this can be confidently stated.

8. There seems to be some tendency for the chest in pulmonary tuberculosis to acquire a larger or smaller index—*i. e.*, to divide into two types; one flat (index 68 to 70) and one deep and round (index 78 to 80), but both reduced in size.

9. Dr. Hutchinson's normal index appears to be too low, his tuberculous index too high. For far-advanced cases his tuberculous index is probably correct.

10. The relation of the diameters (*i. e.*, the index) does not appear to have any prognostic value, as at either extremes there is no tendency in early cases of pulmonary tuberculosis to show an unduly large proportion of extreme indices.

11. The change of index in pulmonary disease is probably not due to emaciation, but to change in bulk of the lungs.

12. During Sanitarium residence there is marked increase in both expansion and respiratory movement, more striking in advanced than in incipient cases.

This study would have been impossible but for the kindness of a number of our friends. Among them we wish to thank for the unfailing courtesy which they showed us Drs. Woods Hutchinson, D. A. Sargent, J. W. Seaver, Richard Dutton, and C. C. Stroud.

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PULMONARY STREPTOTHRICOSIS.

NOTES OF A CASE WITH CLINICAL PICTURE OF PULMONARY TUBERCULOSIS. SPUTUM CONTAINING AN ACID-RESISTING STREPTOTHRIX. NO TUBERCLE BACILLI.

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During recent years a number of observations have greatly advanced our knowledge concerning the genus *Streptothrix* and the pathology of streptothrix infections. Thirty or more species of streptothrices have been described and the cultural characteristics of the majority fairly well determined, so that some definite light has been thrown upon the confusion in which this particular group of micro-organisms has been involved.

Several points in particular appear to have been decided by this recent work. In the first place, a greater tendency toward unanimity in terminology has been shown. The terms *Actinomyces*, *Cladothrix*, *Oospora*, *Nocardia*, and *Streptothrix* have all been used as generic synonyms for branching mycelial organisms, but in the last two or three years a decided preference has been manifested toward discarding of the older terms in favor of the term *Streptothrix*. The majority of pathologists seem to be following this usage, though some prefer to cling to the older and more proper designation *Actinomyces*. But as *Actinomycosis*, instead of being a single disease-entity caused by a single micro-organism (*Actinomyces bovis*, Harz and Bollinger), has been positively shown to be a variety of infections due to different species of streptothrix, there are some very good reasons for abandoning the use of the term actinomycosis, at least in the pathological sense, in favor of the term *Streptothricosis*. The former term, though the older, can at present retain only a broad clinical significance as a designation for a class of diseases caused by related but distinct specific organisms.

Actinomycosis in man appears in the majority of recently reported cases to be due to other forms of streptothrix than the common one infecting cattle (*Streptothrix* [*Actinomyces*] *bovis communis*). Indeed, the cattle disease is most probably a varied infection caused by several species of streptothrix. Should the study of a greater number of cases prove this to be generally true, it should be more advisable not to designate these different infections by one and the

same clinical term. Still further ground is found for this in the fact that these different forms of streptothrix infections are not clinically identical, but present important differences in so far as symptoms, prognosis, and treatment are concerned. As to the designation of those streptothrix infections which are not caused by the common one of cattle under the head of pseudoactinomycosis or pseudotuberculosis, little need be said. There is a nearly general unanimity of opinion as to the impropriety of these terms. Manifestly at present the best way out of the difficulty is to class all streptothrix infections under the general heading of *Streptothricosis*, giving the specific name of the particular organism causing the infection. At the present time the cultural identification of the organism causing these conditions is of the greatest importance, and until this has been accomplished in a large number of cases we shall have little foundation upon which to base a definite clinical and pathological conception of these infections. With the accumulation of well-studied cases it is possible that some more satisfactory system of nomenclature may be devised.

Among the recently reported cases of human infection with streptothrices, there stands out prominently a small but exceedingly interesting group of pulmonary cases presenting the clinical picture of tuberculosis, bronchopneumonia, or gangrene, but in which the infecting agent appears to be some form of streptothrix differing from *Streptothrix bovis communis*. Not only have these cases been shown to be associated with different species of streptothrix, but they have also presented clinical and pathological characteristics quite different from pulmonary actinomycosis when caused by the cattle streptothrix. While there can be no doubt that pulmonary infections with the latter organism have actually occurred in man and have been correctly diagnosed, it is very probable, in the light of recent studies, that only a small proportion of the cases in man described as actinomycosis have been due to this particular organism.

Eppinger[1] isolated a streptothrix having well-marked cultural characteristics from a patient, a glass-polisher, aged fifty-two years, who had been treated for "cerebrospinal meningitis." Autopsy showed an abscess in right cerebral hemisphere which had discharged into the lateral ventricle, calcification of the bronchial and supraclavicular glands, old caseous nodules in apices of lungs, and a "pseudotuberculosis" of lungs and pleura. The streptothrix was isolated from the pus of the cerebral abscess. Inoculation of the pure culture into guinea-pigs and rabbits produced a "pseudotuberculosis." The organism was first designated *Cladothrix asteroides* by Eppinger, but has been since classed as *Streptothrix eppingeri* (Kruse). It does not liquefy gelatin or inspissated horse serum, and has no diastatic action on starch in peptone solution. On maltose agar the growth is at first of a yellowish-white color, then becomes

of a deeper yellowish to a yellowish-red. On potato the growth is at first whitish, then becomes of a yellow to a brick-red color, and shows a fine, powdery efflorescence on the surface. Reaction of alkaline litmus milk not changed after twenty days' incubation. Portions of the mycelium are acid-fast, but not alcohol-fast.

Sabrazés and Rivière[2] report 2 cases of human streptothricosis in which the lung was involved. In the first case a branching filamentous organism was found in the pus from cerebral and kidney abscesses in a young man, who also presented pulmonary abscesses. The organism, however, was not found in the latter. The organism stained with Gram's, and in anaërobic cultures produced white, cloudy colonies of streptothrix. In the second case a streptothrix was obtained in a pure culture from the sputum and the pus of subcutaneous abscesses. It was aërobic, liquefied gelatin, and produced a yellow pigment. It was not pathogenic to animals unless inoculated in association with lactic acid.

Buchholz[3] reports a case of a steel-worker, aged thirty-eight years, presenting the clinical appearance of tuberculous pneumonia and empyema. The sputum contained streptococci, but no tubercle bacilli. Autopsy showed extensive pleural adhesions, and empyematous cavities communicating with cavities in the lung tissue. These resembled tuberculous cavities, except in possessing more ragged walls. The tissue about the cavities was consolidated and presented necrotic and atelectatic areas. Microscopically the consolidated areas gave the appearance of a fibrinous pneumonia rather than of a tuberculous process. Staining with Gram's showed throughout the necrotic tissues around the cavities a thick network of delicate branching threads of about the same thickness as tubercle bacilli. The filaments showed occasionally interrupted staining, with here and there a thickening, but no coccoid or bacillary forms. Streptococci were not found in the infiltrated and necrotic parts, but were present in the atelectatic regions. Tubercle bacilli were not found. Buchholz, therefore, believes that the streptothrix was the cause of the lobular pneumonia and resulting necrosis, and that the streptococcus invasion was secondary. Cultures were not successful, the plates being overgrown with a variety of proteus. Animal experiments were not carried out. No mention is made of the staining properties of the organism as regards its acid or alcohol resistance. He regarded the organism as identical with or related to that of Eppinger.

Scheele and Petruschky[4] describe the case of a woman, aged fifty-six years, who, after an attack of influenza, developed a condition characterized by irregular fever, pain in the left side, and multiple subcutaneous abscesses, occurring particularly in the neighborhood of the joints. After three months' illness death occurred, and the autopsy showed left-sided pleuropneumonia, cardiac dilatation, splenic enlargement, cystitis, and pyelitis. From the sputum and

the pus of the subcutaneous abscesses there was obtained a streptothrix in pure culture, which, on agar, formed pure, white colonies, having a characteristic odor. Growth was also obtained on gelatin and in bouillon, but not on potato or on glucose agar. In the sputum the organism proved acid-fast when stained by Gabbett's method. This case is the first in which pulmonary streptothricosis was diagnosed during life.

Petruschky[5] refers to a second case in which a similar organism was isolated from the sputum of a child thought to have tuberculosis. This organism differed from that described above in giving a more abundant growth and causing liquefaction of the gelatin.

Rullmann[6] reports a case in which there was a localized lesion near the root of the right lung (bronchial gland?) associated with the presence of a streptothrix in the sputum, occurring in tough, yellowish-green masses, consisting of interlacing filaments in pure culture. Some of the filaments showed true branching. They stained well with ordinary bacterial stains and with Gram's. Pure cultures were obtained, the organism growing well on all ordinary media. On blood serum it formed chrome-yellow colonies; in bouillon a good surface growth with later turbidity. Aërobically on solidified egg-albumen it produced filaments; anaërobically rods with club-shaped ends like diphtheria bacilli. The cultures possessed a mouldy or earthy odor. Inoculation into various animals gave positive results, the organism being recovered from the lesions. Suppuration of the lymphatic glands was the most striking feature of the infection. Only the filamentous form was found in the inoculated animals.

In 1902 Rullmann[6] reports further observations upon the sputum of this case. In the expectorated granules the same organism was found, partly in pure culture and partly in association with other bacteria. On Loeffler serum it formed chrome-yellow cultures, in part whitish, and resembled diphtheria cultures. In the cultures the organism showed clubbed ends and true branching. Bouillon was not clouded. On gelatin the growth was slow. A skiagraph showed three circumscribed shadows at the root of the left lung (areas of induration?), pleural shadow and diminished diaphragmatic movement on right.

Flexner[7] has studied very carefully a case of pulmonary streptothricosis in a colored man aged seventy years, closely resembling Buchholz's case, both in the clinical history, morbid anatomy, and morphological characteristics of the organism found in the lesions. The clinical picture was that of pulmonary tuberculosis. No sputum was obtained. Autopsy showed partial consolidation of both lungs, with caseous and calcareous nodules and early stage of cavity formation. The pleura over the fresh foci of consolidation was covered with fibrin and studded with small hemorrhages. Over the peritoneal surfaces, especially in the omentum, numerous nodules resembling tubercles were found. Similar nodules were present in the

liver and spleen. The mesenteric glands were not enlarged, but on section showed minute tubercles. Microscopically the sections of the lungs showed a cellular exudate in part, and in part a fibrinous one. The alveolar walls themselves were infiltrated with polymorphonuclear leukocytes. These showed marked disintegration, in some areas to the extent of softening and cavity formation. Circumscribed nodules having the size, form, and appearance of miliary tubercles were present. They consisted chiefly of epithelioid cells; giant cells were not found. These were present, however, in the peritoneal nodules, which very closely resembled tubercles in their structure. Throughout the diseased areas there was found a filamentous organism often in convoluted masses. The branches were sometimes capped by a conical swelling. The filaments in part stained irregularly, giving a beaded appearance. Rarely they showed a tendency to break into small rods. In the peritoneal nodules the organism appeared more in the form of rods with a marked tendency to beading. The organism stained well with Weigert's modification of Gram's, and in section stained with Gabbett's method retained the carbol-fuchsin to some extent. Cultures and inoculations were negative. No tubercle bacilli were found, and the inoculated guinea-pigs showed no evidences of tuberculosis. Flexner styled the process *pseudotuberculosis hominis*, and the organism *Streptothrix pseudotuberculosa*. He regards it as probably identical with the one described by Buchholz; and the latter, after seeing Flexner's slides and comparing these with his own, regarded the two organisms as probably identical.

Foulerton[8] reports a case of an Italian woman, aged forty-six years, having a history of chest trouble for ten years. The symptoms had increased in severity during the two years immediately preceding admission. Abscesses were present in the left axilla and above the left clavicle, and there was a marked induration of the subcutaneous tissues about the left shoulder. In addition, there were physical signs of extensive disease in the thorax. Large numbers of streptothrix were present in the expectoration and in the pus of the subcutaneous abscesses. From the latter the organism was obtained in pure culture, but could not be positively identified with any previously described species of streptothrix. It was, therefore, classed *Streptothrix hominis* (Foulerton). On nutrient maltose agar it gave a slowly increasing, dry-looking, whitish growth, resembling that of tubercle bacilli. There was no growth on potato or gelatin. On horse serum there was a scanty growth, showing moderate pitting and no actual liquefaction. Diastatic action not tested. Not acid-fast in the one culture examined.

Norris and Larkin[9] have made a very thorough study of 2 cases of bronchopneumonia in man characterized by intense catarrhal and necrotic inflammation of the bronchi and by the presence of numerous streptothrix colonies in the bronchial lumina. Inocula-

tion experiments were positive, and from the empyema pus of a rabbit inoculated from Case II. the streptothrix was finally isolated in pure culture. The organism was grown with great difficulty; solid media, with the exception of rabbit's kidney, being found unsuitable. When finally obtained, the colonies on neutral or 0.5 acid agar were of small size, whitish, and opaque, resembling more nearly bacterial growths than the dry growths characteristic of the streptothrices. On coagulated ascitic serum containing broth and sugar and on Loeffler's serum, a scanty, whitish growth was obtained. In bouillon two varieties of growth were obtained, one with small, hard, and adherent discoid granules, the other of the large, clumpy variety. No growth could be obtained upon potato. The organism stained with Gram's. When stained with hot carbol-fuchsin and decolorized in 97 per cent. alcohol, certain portions retained the red. With weak solution of acids the decolorization was complete. The authors regard their organism as probably identical with or at least closely related to *Streptothrix israeli*, or to the species isolated by Kruse. The pulmonary lesions of these cases, however, did not resemble the bronchopneumonic type of pulmonary actinomycosis described in the literature. The intense necrotic inflammation of the bronchi in the 2 cases distinguished them from previously reported cases of pulmonary actinomycosis or pseudo-actinomycosis.

Aoyama and Miyamoto[10] have reported a case of pulmonary streptothricosis in which the sputum and the pus from a cavity in the lung contained branched threads, which they described as being "as acid-fast as tubercle bacilli." From the pus in the lung cavity a pure culture of streptothrix was obtained. It stained by Gram's and by Gabbett's methods, the threads not staining equally, but portions remaining unstained. Anaërobically the growth was very scant. On glycerin-agar the developing colonies were whitish; in older colonies the centre was dark, opaque, and yellowish, with a thinner, whitish margin. On blood serum the growth was scanty and of a yellowish color. In bouillon fine, grayish-white, chalky colonies appeared on the surface; these became coherent and sank to the bottom as a flocculent precipitate, having a mother-of-pearl sheen. In old cultures the broth took on a brownish tinge. On potato the growth was at first white, but after a time became brownish, forming a loosely friable mass. Inoculations were positive; grayish-white nodules containing the streptothrix were found in the lungs, heart muscle, kidneys, spleen, brain, and on the peritoneum of the experimental animals. In a pregnant guinea-pig the organism was recovered from the blood of the placenta. The very full account given of this organism by Aoyama and Miyamoto makes it highly probable that it is identical with *Streptothrix eppingeri*. They themselves regard it as probably identical with the one described by Buchholz, but as the latter organism was not isolated, an absolute

identification becomes impossible. To the organisms described by Petruschky and Rullmann it has no resemblance.

Aoyama also states that in 1899 he had made an autopsy on a body dying of a condition diagnosed during life as tuberculous hemorrhagic pleuritis and kakke. In the hepatized portion of the lung numerous streptothrices were found.

Musser[11] reports a case of pulmonary streptothricosis in a man, aged thirty-seven years, suffering from bronchial symptoms and fever, and dying finally from bronchopneumonia. There was no leukocytosis, the leukocyte count being 3200. Streptothrical filaments and streptococci were found in the sputum. No cultures were obtained. The author was unable to decide whether the case was one of primary streptothrical infection or of primary streptococcus infection with secondary streptothrix infection, or whether the organisms described were branched tubercle bacilli.

Mayer,[12] in his "Briefe aus Ostasien," mentions 10 cases having pronounced symptoms of tuberculosis in which an acid-resisting and moderately alcohol-fast streptothrix was found in the sputum, pleuritic fluid, and in smears and sections from the pulmonary foci. He regarded these organisms as having the same significance as the acid-resisting bacilli found in pulmonary gangrene by Fraenkel, Pappenheim and Rabinowitsch.

Ohlmacher[13] describes an atypical acid-fast and alcohol-fast organism obtained from the sputum of a case clinically resembling pulmonary tuberculosis. Cultures could not be obtained, and inoculation experiments were negative. The inoculated animals showed no evidences of tuberculosis. The morphology of the organism as seen in the stained specimens of sputum corresponded neither to the tubercle bacillus nor the smegma bacillus, but was somewhat suggestive of Flexner's *Streptothrix pseudotuberculosa*, except in being a much more delicate organism. The author was unable to classify it, but was inclined to place the organism with the cases of Pappenheim, Fraenkel, and Rabinowitsch, in which acid-resisting bacilli resembling the tubercle bacillus were found in association with the pathological picture of chronic bronchitis and pulmonary gangrene.

Birt and Leishman[14] isolated a new streptothrix from the sputum and pleural effusion of a young man suffering from hectic fever and right-sided pleuritis, attended by the expectoration of a mucopurulent material. Autopsy showed an advanced empyema on the right side and a condition of chronic bronchopneumonia. Throughout the lung there were numerous small, hard nodules, showing no caseation and differing in many respects from miliary tubercles. The streptothrix was obtained in pure culture from the pericardial fluid and in connection with pyogenic organisms from the empyema pus and the nodules in the left lung. It grew very slightly at room temperature. In the incubator it grew rapidly on gelatin without liquefaction. On agar the growth was rapid, forming a

snow-white, dry, powdery material, taking on a pale coral-pink tinge after a few days. On potato a growth was obtained resembling a splash of plaster of Paris. There was no growth on blood serum. With Gabbett's method the organism was acid-resisting. It occurred both in branching threads and in the streptococcoid form. Inoculation showed it to be pathogenic for guinea-pigs.

Ophüls[15] reports 5 cases of pulmonary gangrene in which acid-resisting bacilli were found. True branching forms were found in all cases. Pure cultures were not obtained, and animal experiments were not carried out. It was impossible to decide whether the organism in all cases belonged to the same species. The author believed that they were certainly closely related and probably belonged to the class of acid-resisting bacilli found in butter, on timothy grass, etc. He would, therefore, class his cases with those reported by Fraenkel, Pappenheim, Rabinowitsch, Benvenuti, etc. He further suspects that the acid-proof bacilli come from the mouth.

Of the cases abstracted above, it is very probable that those of Mayer, Ohlmacher, and Ophüls belong to a separate class and are to be put by the side of the cases of acid-resisting bacilli reported by Fraenkel, Pappenheim, Rabinowitsch, etc. It is also a question if the organism described by Norris and Larkin may not also belong to this class. The authors themselves regarded it as closely related to *Streptothrix israeli.* The meagreness of description in Musser's case and his own doubt as to the character of his organism make its classification impossible. Of the other cases, Buchholz regarded specimens of Flexner's streptothrix as identical with his own, which he thought might be the same as Eppinger's. Aoyama and Miyamoto regard theirs as probably identical with the one of Buchholz; but Foulerton thinks from their very full description that it is identical with *Streptothrix eppingeri.* If we take the morphological descriptions alone the organisms of Buchholz, Flexner, and Aoyama and Miyamoto certainly fall into the same class. The failure of cultivation in the cases of Buchholz and Flexner make the final classification of their organisms impossible. On the other hand, the organisms described by Sabrazés and Rivière, Scheele and Petruschky, Rullmann, Foulerton, and Birt and Leishmann are distinct from *Streptothrix eppingeri* and probably from each other. It is apparent then that a variety of streptothrices are concerned in pulmonary infections, but that it is impossible at the present time to classify these definitely, either according to their morphological and cultural characteristics or from a pathological or clinical standpoint.

Such being our state of knowledge upon this subject, the report of every case of pulmonary streptothricosis observed becomes an imperative duty at this time. We add, therefore, to the casuistics of this subject the following case, which, though incomplete, lacking culture and inoculation experiments and autopsy, is of great importance in confirming the cases of Buchholz and Flexner, and in

showing the wide geographical distribution of this form of pulmonary streptothricosis:

History of Case. (Furnished by Dr. King, of Pueblo, Colorado.) —Mr. J. B., Austrian by birth, aged forty-five years, came to this country when a child and has since lived in Southwestern Kansas. He is married and has several grown children. No family history of tuberculosis. The patient has worked as a farmer for the greater part of his life, and, while never appearing especially robust, has been wiry and a hard worker. Three years ago his present trouble began with an attack of "la grippe," after which a moderate cough and expectoration persisted. In consequence he gradually became much weakened and emaciated, and suffered so much from digestive disturbances that he was finally compelled to live upon milk diet alone. In spite of his increasing weakness, he kept at work until six months ago, when he gave up completely and was sent to Colorado with the clinical diagnosis of tuberculosis.

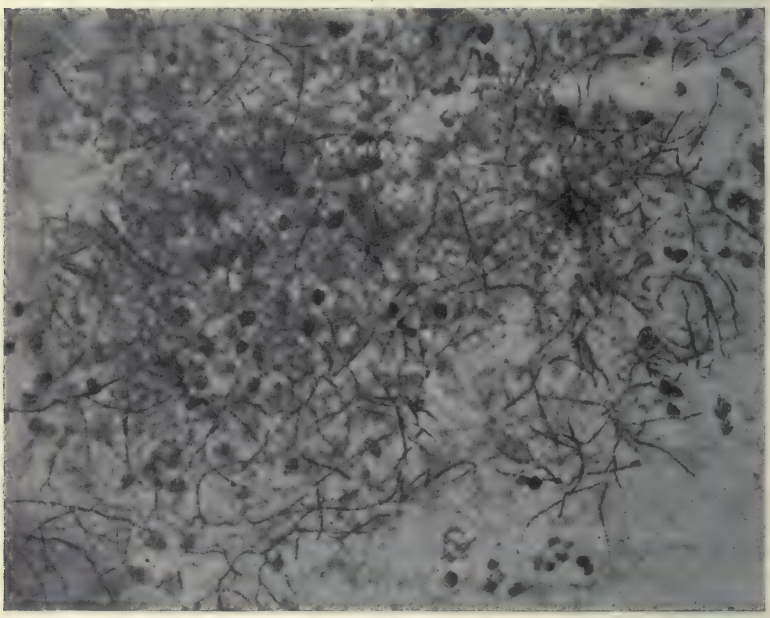
The physical examination (Dr. King) showed good and symmetrical expansion on both sides. No areas of dulness were present and no signs of cavities. The respiration was labored, and on auscultation blowing breath sounds and dry crepitant rales were heard all over the chest. The sputum was raised with difficulty. It was mucopurulent in character, yellowish, and had no disagreeable odor. There was no fetid odor to the breath. The temperature ranged from 102° to 103°. The clinical picture on the whole suggested a chronic bronchitis or bronchopneumonia of tubercular origin.

The sputum was collected and sent to Dr. Olney for examination for tubercle bacilli. The specimen consisted of about one ounce of a yellowish-gray, nearly homogeneous, and somewhat gelatinous sputum, containing great numbers of minute grayish granules. It was easily spread, not stringy, but inclined to make rather thick smears. No blood streaks were seen in it, and it had no noticeable odor. The small grayish granules became more prominent in the dried covers. On the examination of the unstained fresh sputum, it was found to be moderately rich in pus cells. No yellow elastic tissue was found. No blood or pigment cells were present. The small grayish granules proved to be masses of a filamentous organism closely interwoven and branching freely. In the covers stained with carbol-fuchsin Dr. Olney was surprised to find that the branching threads would retain the stain after treatment with 25 per cent. of sulphuric or nitric acids, but gradually lost the red when washed in 95 per cent. alcohol. With the acid alone they were "as acid-fast as the tubercle bacillus." With Gram's the branching threads stained beautifully, standing out in sharp contrast against the clear background.

The unusual character of the organism was at once recognized by Dr. Olney, who suspected that the case was one of actinomycosis.

He therefore made a careful search for characteristic "Drusen," but failed to find anything at all resembling these. A very thorough search was also made for the tubercle bacillus, but none were found. With the exception of a very few streptococci and staphylococci, the only constituents of the sputum were the filamentous organism and pus cells. Convinced, therefore, that the case was one of infection with some rare member of the streptothrix group and not having access to the literature, Dr. Olney sent his preparations to the Pathological Laboratory of the University of Michigan for diagnosis. In the mean time, he at once made arrangements for securing cul-

FIG. 1.



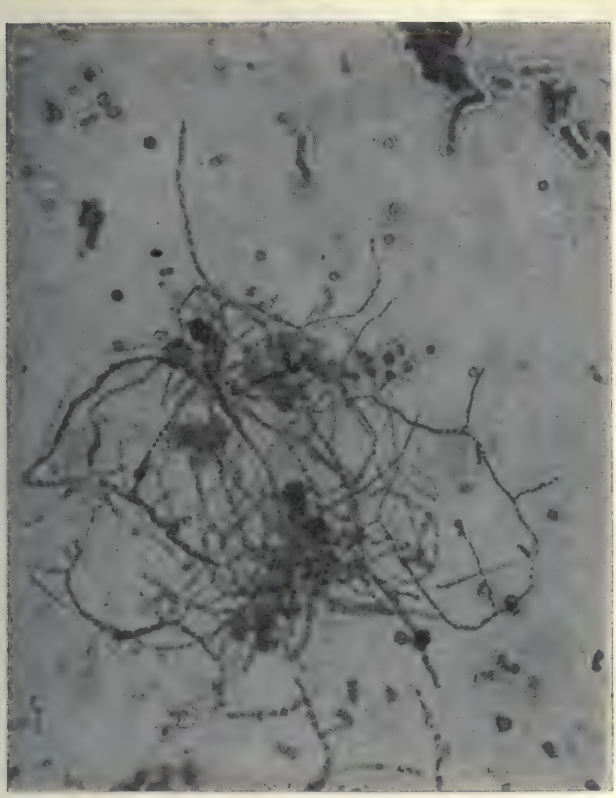
Small grayish mass from sputum, consisting of tangled streptothrix threads, puss cells, etc. × 300.

tures, but, unfortunately, the patient had suddenly become much worse, and had been taken by his friends to a tuberculosis sanitarium, where he died on the second day after the first sample of sputum had been sent to Dr. Olney. No autopsy was permitted. No history of the case was taken at the sanitarium, nor was any examination of the sputum made there.

The specimens received from Dr. Olney consisted of smears of sputum stained with carbol-fuchsin (acid decolorization) and by Gram's method. In every field there was present a filamentous organism showing true branching. Usually the threads were

entangled, interwoven masses somewhat convoluted, but occasionally single branching filaments were seen. The filaments varied in length, but many extended across several oil-immersion fields. The length of the branches also varied greatly, but the majority were short. No conical or club-shaped terminations were seen. The filaments also varied in thickness, the majority being about four times as thick as a tubercle bacillus, though some threads had about

FIG. 2.

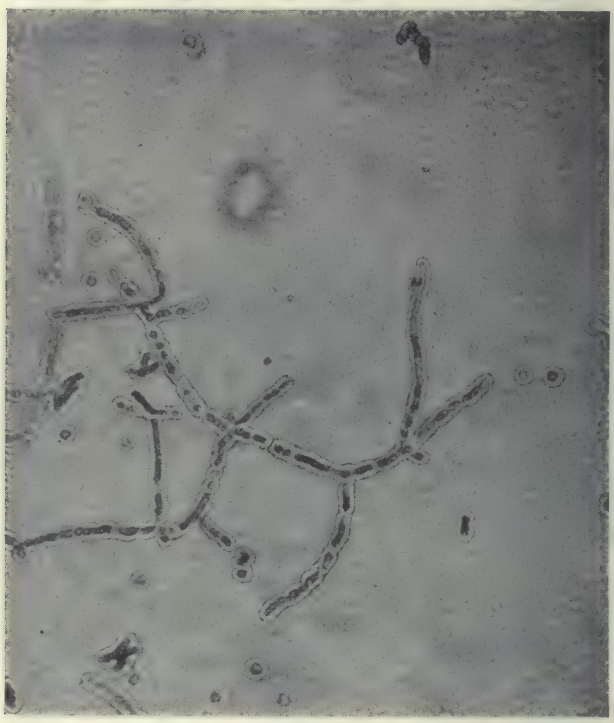


Mass of streptothrix threads from sputum, stained with carbol-fuchsin and decolorized in 25 per cent. nitric acid. All the threads acid-fast. × 750.

the same thickness as the latter. No bacillary or coccus-like forms were found. In the specimens stained with carbol-fuchsin and decolorized with acid, the majority of the threads presented a beaded appearance or seemed to be breaking up into short rods of varying length. The staining of the beaded threads is very irregular, and the beaded appearance seems to be dependent upon the degree of decolorization. The deeply staining threads are wider than the lighter ones, and by focusing a clear unstained protoplasm may be

seen connecting the stained portions. The unstained portions are somewhat wider than the stained. In the smears stained with Gram's the beading is not so marked, although by longer decolorization it becomes more evident. It would seem, therefore, that the beading is more or less dependent upon the staining procedure. Pus cells were found in moderate numbers in the mesh of threads, many mononuclear cells being present. Streptococci and staphylococci were present in small numbers.

FIG. 3.



Streptothrix threads from sputum, stained with carbol-fuchsin and decolorized in 25 per cent. nitric acid, showing true branching and beading. × 1200.

From the above characteristics it was at once evident that the organism was a streptothrix, morphologically identical with the ones described by Buchholz and Flexner. This opinion was confirmed by Dr. Flexner, to whom stained smears were shown. There can, therefore, be but little doubt that this case was one of pulmonary streptothricosis, even in the absence of autopsy confirmation, and that it is to be classed with those of Eppinger, Buchholz, Flexner, and Aoyama and Miyamoto. In the absence of definite knowledge

concerning the cultural characteristics of the organism in the cases of Buchholz and Flexner, as well as in our own, no absolute identification of the species of streptothrix is possible, but it seems very probable that in all of these 5 cases either the *Streptothrix eppingeri* or a very closely related species is to be regarded as the cause of the infection.

We must conclude, therefore, from these 5 cases that there is a distinct form of pulmonary infection clinically resembling tuberculosis and caused by an acid-resisting streptothrix having a wide, geographical distribution. The existence of such a condition becomes of great importance, in so far as the question of the differential diagnosis of tuberculosis is concerned. The frequency of occurrence, the symptomatology, and the therapeutics of this form of streptothricosis remain yet to be worked out, and it is highly desirable that those happening to meet such cases should make a thorough investigation as to these points and also as to the cultural characteristics of the infecting organism.

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TUBERCULOSIS AND HEART DISEASE.

BASED UPON THE STUDY OF 1764 AUTOPSIES, 1276 CLINICAL HISTORIES, AND A REVIEW OF THE LITERATURE.

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Having within the last year had the opportunity of examining all the post-mortem records at three of the hospitals in Philadelphia, aggregating a total of 7040, I have collected data from all those which showed tuberculous lesions of the lungs, pleura, peri-

cardium, heart, and great vessels, with a view of studying their frequency and relationship.* Statistics have also been gathered upon 57 successive cases of valvular heart disease which have come to autopsy at the Pennsylvania Hospital. The individual totals from the different hospitals are summed up as follows:

	Total autopsies.	Tuberculous cases.	Per cent.
Philadelphia Hospital	6426	1606	26
Pennsylvania Hospital	562	106	18
Phipps Institute	52	52	100
	7040	1764	

Tuberculous pericarditis has been considered in a previous paper,† and will be omitted from the present one; it may be stated, however, that the condition is a relatively common one, it having been encountered 81 times in 1780 (4.4 per cent.) tuberculous autopsies; while in 31 additional cases of undetermined etiology tuberculosis may have been the causative factor. Small localized areas of inflammation—milk spots—were not included in the foregoing enumeration.

The earliest work dealing with the relationship of pulmonary tuberculosis and heart disease which I have been able to find dates back to 1806, the year in which Corvisart in his essay "On Diseases of the Heart and Large Vessels" described the existence of small hard tubercles situated on the mitral valve. But the subject did not attract much attention until Rokitansky, in 1846, first enunciated the doctrine of antagonism between valvular heart disease and tuberculosis of the lungs, claiming that the existence of chronic endocarditis virtually precluded the latter disease, and explaining this immunity by the congestion and stagnation of venous blood in the lungs.

Following out this line of thought Rokitansky[12] and his disciples taught that valvular disease of the heart, especially when affecting the mitral or aortic valves, as well as aneurysms of the large vessels, hydrothorax, and even scoliosis, lessened the tendency to pulmonary tuberculosis. This idea that scoliosis conferred a relative immunity is interesting in the light of modern research, especially in connection with preventive inoculation. The increased resistance to tuberculosis in individuals with scoliosis probably exists, not by reason of venous stasis, but because patients who have recovered from an attack of tubercular bone disease have usually developed an inhibitory capacity to tuberculosis of considerably greater potency than that possessed by an unaffected organism. Certainly it would seem to be an established fact that patients of the so-called scrofulous class often show an increased resistance to tuberculosis, which

* I am indebted to Drs. Biggs and Longcope, respectively, for having placed at my disposal the autopsy records of the Philadelphia and the Pennsylvania Hospitals.

† University of Pennsylvania Medical Bulletin, 1904.

if it gains foothold in the economy often runs the protracted course of a disease implanted upon an unfavorable soil.

Rokitansky's doctrine held unchallenged sway until Traube,[13] in 1864, reported a series of cases in which aortic disease and phthisis pulmonalis were coincidently found at autopsy. The last-named author, however, admitted the extreme rarity of such coincidence, but believed that mitral stenosis was directly inhibitory. Three years later corroborating though modifying evidence was added to the antagonism doctrine, when Lebert[14] reported 24 cases of pulmonary stenosis (15 in men, 9 in women), all of whom were the subjects of pulmonary tuberculosis, and most of whom died of the latter disease without having a tubercular heritage, before reaching the age of twenty-five. If Rokitansky's views were correct and venous stagnation prevented tuberculosis, it seemed but natural to believe that the anæmia of pulmonary stenosis should favor it.

It was not until 1875 that the antagonism theory received undeniable disproof. In this year Frommolt,[15] in a paper based upon 7870 autopsies made in Dresden in the course of twenty-five years, reported 277 (3.5 per cent.) cases of valvular heart disease—all but 1 lesions of the left heart—among which 22, or 8 per cent., had pulmonary tuberculosis. Following the footsteps of Frommolt, Niemeyer, Ruehle, Lepine, and others adduced corroborating evidence and succeeded in quite thoroughly discrediting the absolutism of Rokitansky's teaching, although many authorities still insist on the rarity of coincident tuberculosis and disease of the heart. Certainly the trend of modern belief is to set but little if any faith in the immunizing effect of chronic endocarditis, a fact which is no doubt due largely to the increasing accuracy and thoroughness of our pathological research.

Another belief held by Rokitansky, and before him by Laennec,[111] Louis,[112] and Bizot,[16] was that pulmonary tuberculosis usually if not always occurred in individuals with small hearts. Louis, in 112 autopsies upon tuberculous individuals, found the heart enlarged only three times; in about one-half of the cases it was subnormal in size. Beneke[1] met with similar results in a large number of cases, and believed the condition to be due to a congenital hypoplasia, in which the vascular system shared. Potain,[2] while admitting the fact, attributed the smallness of the heart to impoverished nutrition. Reuter,[3] in a series of 251 autopsies, encountered the following state of affairs:

Small hearts	men	29.0 %
	women	56.0 %
Normal hearts	men	30.7 %
	women	23.2 %
Large hearts	men	40.2 %
	women	20.0 %

Hirsch,[4] on the other hand, found the heart enlarged in 44 per cent. of his tuberculous cases, and abnormally small in only 5 per cent.,

the increased size being due to an hypertrophy of the right ventricle. The doctrine that cardiac hypoplasia was a potent factor in the predisposition to tuberculosis was enthusiastically heralded by Brehmer,[5] who was impressed with this belief by observations made upon the inhabitants of Goerbersdorf—a mountainous resort in which rarefied air conduced to hypertrophy of the heart—among whom tuberculosis was extremely rare. Brehmer believed that the small heart of tuberculous individuals was the result of malnutrition during the period of growth, a condition which is evinced by the poor appetites of scrofulous children, who as a result do not attain a normal body weight. He tried to substantiate his dictum by the results of investigations which had been made upon growing animals, it having been shown that strong, well-fed, healthy oxen possessed smaller lungs in proportion to their body weight than did the less robust specimens, in which the hearts were relatively smaller in comparison to the lungs. Spatz[6] has collected statistics from 327 tuberculous autopsies in which the relative size of the cardiac orifices, wall, and chambers were carefully recorded. He found the heart in the majority of instances smaller than normal, with a tendency to left ventricular hypertrophy. The aorta was often found subnormal in calibre, especially in women. One case in the present series derived from the records of the Pennsylvania Hospital showed congenital atresia of the aorta, which had been found in an adult negro who died of pneumonia and who had never been conscious of cardiac insufficiency. The systemic circulation had been carried on through a patent and enlarged ductus arteriosus; there was no evidence of pulmonary tuberculosis. Oppenheimer's[7] studies showed that the greatest disproportion between the human heart and body existed at the time of puberty, a time when tubercular manifestations are very common. When enlargement of the heart is found in pulmonary tuberculosis it is often due to the use of alcohol (Bauer and Bollinger,[8] Reuter[3]) or to a coincident nephritis, it being therefore more frequently encountered in men. A more recent study of this subject has been made by Bouchard and Balthazard,[9] who have estimated the size of the heart in 90 living cases of pulmonary tuberculosis by means of the fluoroscope and radiographic screen which is held at different angles to the body. The results thus obtained were compared with: (1) the bodily height; (2) the frontal size of the thorax; (3) the weight of the individual; (4) the "fixed albumin" before emaciation, *i. e.*, the weight which a person of the same age, size, and musculature would have under normal conditions. The results of these investigations showed two classes of consumptives: 1. Those who had contracted tuberculosis, though not predisposed. 2. Those who were predisposed. In the first class the heart was normal in size; in the second, this organ possessed only one-half of its natural proportions; in other words, the heart had 0.5 sq. cm. less area for every kilogram

of fixed albumin than would have been the case in a normal individual. In the third stage of pulmonary tuberculosis this standard was raised through cardiac dilatation, the increase in size being indicated by about 10 sq. cm. in the total area as compared with the early stages of tuberculosis. In other chronic diseases this smallness of the heart was not found. Regnault[10] denies that the heart is atrophied in chronic pulmonary tuberculosis, and calls attention to the frequency with which dilatation or hypertrophy of the right ventricle is encountered. Fraenkel[11] comments upon the fact that this right ventricular dilatation is occasionally more easily demonstrable during life than at autopsy, and suggests as a reason the fact that during the last stages of the disease the blood pressure is lowered and the whole volume of the blood decreased. In the present series of cases the weight of the heart was recorded in 1269; it was found to be enlarged, *i. e.*, weighed over 380 gr., 217 times; in 161 of these the enlargement was associated with and presumably due to valvular disease or pericardial adhesions. The remaining 56 instances of hypertrophy were in a considerable number of instances apparently due the coincidence of chronic nephritis. The exact location of the cardiac enlargement was not regularly recorded, but such information on the subject as was obtainable resulted as follows: general hypertrophy, 41; right-sided hypertrophy, 20; left-sided hypertrophy, 38. The heart of adults was found to weigh less than 200 grams in 184 instances, leaving 707 normal-sized hearts. Hypoplasia of the aorta was met with three times. The following pathological cardiac conditions were also encountered in the 1764 tuberculous autopsies:

Brown atrophy	37	Gumma of lung	1
Fatty degeneration	24	Carcinoma of lung	1
Valvular fenestration:		Acute hemorrhagic myocarditis	1
Aortic	5	Tuberculosis of the aorta	1
Pulmonary	2	Tubercles on endocardium	5
Patulous foramen ovale	4	Tuberculous endocarditis	2
Abscess of mitral leaflet	1	Tuberculous myocarditis	6

The foregoing figures show that cardiac hypoplasia occurred with but moderate frequency; but it must be borne in mind that the majority of the cases were taken from the records of a hospital in which a large number of the autopsies are made upon individuals who have passed middle life, among whom syphilis and nephritis are common, who die in the almshouse or in the insane wards, with tuberculosis, it is true, but not necessarily of it. The post-mortem examinations at the Phipps Institute, where the majority of the patients are not beyond middle life, showed a very much lower proportion of enlarged hearts. It would seem, therefore, that in uncomplicated cases of pulmonary tuberculosis the heart is subnormal in size in quite a considerable number of the cases. A fact which must, however, not be lost sight of in this connection is that the heart of tuberculous individuals is often small not as the result

of hypoplasia, but from atrophy or degeneration of its substance. This fact has long since been sufficiently pointed out by Louis, Andral, Kidd, Bennet, Quain, Strümpell, v. Leyden, and has been observed by all who have given attention to the matter.

The clinical histories of the Phipps Institute show that among 1276 cases of pulmonary tuberculosis examined, dilatation of the right ventricle was demonstrated in 46. Jaccoud found this condition most frequently associated with large cavities in the lungs. Lebert[103] encountered hypertrophy of the right ventricle in 21 per cent. of the chronic and 13 per cent. of the acute cases.

Taking up Rokitansky's doctrine of immunity—or at least the modified view of it—that of a relative inhibition upon tubercular infection of the lungs—let us see upon what scientific facts such a resistance can be based. Congestion of the lungs when long standing produces an increased dilatation and tortuosity of the capillaries, causing them to project into the alveoli, which in turn brings about an increased transudation of serum. Following upon this, cell proliferation, with slight hypertrophy of the fibrous and muscular tissue, takes place, this being accompanied by an increased deposition of pigment. Here at once we have several causes at work which might inhibit tubercular growth. First, the increased transudation tends to wash out foreign bodies from the bronchioles, also favors cell nutrition and exercises a germicidal effect. Second, fibrous hyperplasia is in itself more or less inhibitive and destructive to tubercle bacilli. This is shown by the clinical course of fibroid tuberculosis, and by the fact that lungs with high grades of emphysema hardly ever show extensive tubercular involvement. Third, the addition of muscular tissue permits more forcible expulsion of extraneous material. "I think it not unlikely that this increase of contractile power may underlie the well-known immunity of the lungs affected with brown induration for such disorders as have their origin in the retention of retained catarrhal secretions." (Rindfleisch.) Based upon this idea that venous stagnation was unfavorable to the growth of the tubercle bacillus, Bier[17] was led to attempt the cure of tuberculous arthritis by means of an artificial stagnation of blood brought about by tightly bandaging the extremities on the proximal side of the lesion. Pearce[18] has lately called attention to the hypertrophy of the elastic fibres in the pulmonary tissues, which occurs in chronic congestion. The latter finding corroborates Hess'[105] contention that the amount and functional efficiency of the pulmonary elastic tissue plays no small part in the resistance of the organism to tuberculosis, the character and extent of the difference in the elastica of contrasted individuals being shown by the very variable degree with which this substance takes certain stains or decolorizes. Fossier,[115] on the other hand, has shown that tubercle bacilli are by no means rarely found in parts of the lungs which are most involved by cyanotic induration.

A search into the voluminous literature of the subject reveals marked differences of opinion and great discrepancies in the statistics. With one accord, however, all authors agree that stenosis of the pulmonary orifice favors the development of tuberculosis of the lungs. This predisposition was first pointed out by Frerichs. His claim was, as has already been stated, placed upon a firm basis by Lebert,[14] and later by Stoelker.[20] The former believed that the results were brought about, not owing to the pulmonary anæmia, as was taught by v. Leyden,[21] but by means of the abnormal and unequal character of the circulation. Fischer[22] attributes the frequency of tuberculosis to the general lack of vitality and resistance which is but to be expected in individuals with congenital malformations. The idea that tubercular infection in these cases was favored by pulmonary anæmia is manifestly erroneous, since the lungs receive their nutrition from the bronchial arteries. The frequency with which pulmonary stenosis is complicated by tuberculosis of the lungs is shown by the following tabulation of collected statistics:

	No. cases of pulmonary stenosis.	No. with pulmonary tuberculosis.
Louis	7	3
Rokitansky	24	10
Gintrac[107]	16	4
Lebert	24	15
Stoelker	116	16
Paul[23]	27	16
Scheele[108]	61	15
v. Carriere[109]	8	4
Peacock[24]	12	12
Schultze[25]	6	5
v. Kryger[26]	2	2
Meisenburg	5	4
Vierordt[110]	83	30
K. v. Ruck[28]	10	10
Babcock[100]	1	1
Burke[104]	47	13

Vierordt has called attention to the fact that the frequent occurrence of tuberculosis is not limited to pulmonary stenosis alone, but is noted also in other varieties of congenital heart disease. This author does not believe that pulmonary tuberculosis is any more frequent in pulmonary stenosis or atresia than is the case in other conditions in which the nutrition is profoundly impaired.

Much diversity of opinion has existed upon the relationship of mitral stenosis to pulmonary tuberculosis. Traube and Lebert held that this form of valvular disease had a distinctly inhibitory, almost immunizing, effect upon pulmonary disease. Teissier,[29] who has written an elaborate monograph upon the subject, denies these statements, but believes that the presence of this form of cardiac lesion favorably influences the course of the pulmonary disease. Similarly to Rokitansky, Potain, Renault, Fraenzel,

Friedreich, Ruhle, Lepine, and others, he attributed this state of affairs to the venous congestion. According to Peter,[30] this modifying influence is brought about by increased functionation of the pulmonary apices which occurs when the bases are congested. It has been suggested by Fischer[22] that mitral stenosis is less frequently encountered in pulmonary tuberculosis, because the duration of life in these cases is, by virtue of the cardiac lesion, necessarily a short one. This is an unsatisfactory explanation, however, because individuals with a double mitral lesion have an equally short, if not shorter, span of life, and yet the two diseases are more frequently coincident in the latter instance than in the former. Meisenburg[27] holds that when mitral stenosis and tuberculosis occur together the former is practically never primary. Fagge[31] states that the last-named variety of heart disease is almost a complete bar to tubercular infection, the statistics of Guy's Hospital having shown only four such cases in a period of thirty years. Walsham[32] found one case of mitral stenosis in 130 tuberculous autopsies, but failed to find this condition in 1000 clinical examinations. The same author in 91 cases which were clinically instances of pure mitral stenosis encountered 3 in which the physical signs might have been those of pulmonary tuberculosis; he does not believe that any definite relationship between the two conditions exist. In Frommolt's statistics of tuberculous cases, mitral stenosis occurred in 5 per cent.; mitral insufficiency in 10 per cent. of the cases. Potain[34] collected 55 instances of mitral stenosis from the autopsy records of the Necker and Charité Hospitals, covering a period of fourteen years, 9 of which showed tuberculous lesions in the lungs. Harris and Beale[33] found mitral stenosis three times in 133 tuberculous autopsies. Fraenkel[11] saw two cases of high-grade mitral stenosis which in the latter stages developed widespread tuberculous lesions in the lungs. Paliard[41] has reported a case of mitral stenosis of rheumatic origin, and of ten years' duration; the patient developed and rapidly died of pulmonary tuberculosis.

A glance at the following tables will show that the coincidence of valvular heart disease and pulmonary tuberculosis is encountered with only moderate infrequency; also that the condition has been more often recorded by recent than by older observers. Clinically the occurrence of valvular lesions has in some instances probably been overestimated, the murmurs heard having been due to other causes than to organic endocardial disease, and the symptoms of apparent cardiac insufficiency to the general systemic weakness, in which the heart muscle shared. On the other hand, slight grades of valvular incompetency are apt to be overlooked at autopsy, especially when the mitral orifice is involved. Varying degrees of endocardial thickening in which the valves take part is a very common finding in chronic tuberculosis; but this condition by no

means necessitates imperfect functionation. In the present series of cases endocardial thickening was found in 15 per cent. of the cases with the following proportion of valvular involvement: mitral, 183; aortic, 126; tricuspid, 23; pulmonary, 13. These cases were not included in those tabulated as valvular disease, among which only such lesions were considered which had been definitely designated by the pathologist as "insufficiency," "stenosis," etc. Teissier found sclerotic endocarditis in 40 per cent. of his tuberculous cases after excluding those which had had other infections. This induration of the endocardium may be generalized, but is usually more marked at the line of valvular contact or at that point of the endocardium at which these structures impinge during diastole. These lesions are most frequently seen on or in the neighborhood of the mitral valve.

Clinical Reports.

Author.	No. tubercular cases.	No. valvular lesions.	Per cent.	Mitral.			Aortic.			
				Insufficiency.	Stenosis.	Both.	Insufficiency.	Stenosis.	Both.	
Phipps' Institute, Philadelphia, 1904.	1,276	76	5.9	45	24	...	3	4	...	
L. Brown,* 1904. Saranac Lake.	600	5	0.8	4	1?	0	0	0	0	1 case mitral insufficiency with doubtful tuberculosis.
J. A. Burroughs,* Asheville, N. C.	4 987	321	6¼	...	...	...	...	...	...	Aortic lesions 32 mitral " 289
J. F. Russell,* Post-Graduate Disp., New York.	1,500	15	1.0	...	...	...	...	...	...	Individual lesions not recorded.
Carrington,* Fort Stanton, N.M.	329	22	6.7	19	1	1	1	1	1	Pulmonary stenosis 1.
E. S. Bullock,* Silver City, N. M.	1,000	20	2.0		...	...	...	...	...	Individual lesions not recorded.
K. von Ruck,* Asheville, N. C.	3,009	43	1.0	21	2	6	2	1	1	Aortic insufficiency complicated by mitral insufficiency 2, pulmon. stenosis 10.
Meisenburg.	4,649	53	1.14	34	0	5	5	2	1	Mitral and aortic insufficiency 2, pulmon. stenosis 4.
J. M. Anders,[35]	94	6	6⅜	4	2	0	0	0	0	
Milliken,†	60	3	5.0	2	1	0	0	0	0	
A. Abrams,†	800	21	2⅝	9	3	3	0	2	0	Pulmonary stenosis 1, unclassified 3.
E. Baldwin,†	1,200	9	¾	7	1	0	1	0	0	
Turban,[36]	408	8	1.9	5	1	0	0	1	1	
Fischer, Wallis,[22]	597	6	1.0	2	1	1	0	0	0	Pulmonary stenosis 2.
Planegg Sanitarium,‡ Munich.	812	8	0.9							
Basler Sanitarium,‡ Davos.	1,030	9	0.8							
Wald Sanitarium,‡ Zurich.	506	4	0.7							
Cotton,[38]	1,000	2	0.2							
A. Eyman,[19]	27,653	80	0.2							Individual lesions not given.
Roepke,[114]	300	3	1.1	3	0	0	0	0	0	

* Personal communication. † Quoted by Anders. ‡ Quoted by Fischer.

The records gathered from the Philadelphia Hospital showed a relatively larger number of aortic lesions than did those from the other institutions, a result which is easily explained by the fact that more of these cases were advanced in life. The patients at the Phipps Institute, on the other hand, were mostly young, their death with a few exceptions having been due to the last-named disease.

STATISTICS FROM AUTOPSIES UPON CASES OF PULMONARY TUBERCULOSIS.

Author.	No. autopsies.	No. valvular disease.	Per cent.	Mitral.			Aortic.			
				Insufficiency.	Stenosis.	Both.	Insufficiency.	Stenosis.	Both.	
Kidd,[37]	500	27	5.4	16	1	1	11	0	2	Tricuspid 2.
Carrington,*	38	8	21.0							
Cotton,[38]	503	55	7.0							
Saenger,[81]	469	3	0.64							
Willigk,[39]	1317	1	0.08							
Reissner,	152	0	0							
Chambers,[40]	566	0	0							
v. Kryger,	1100	10	0.9	3	1	...	4	...	1	Aortic and mitral insufficiency 1.
Otto,[43]	185	29	1.5	...	...	...	...	...	...	Endocardial thickening, especially mitral.
Fenwick,	1560	30	1.9	14	5	0	9	5	0	Endocardial thickening in 12 per ct., 13 acute lesions not definitely.
Norris,	1764	130	7.3	51	14	11	37	9	18	Tricuspid stenosis 2, tricuspid insufficiency 12, pulmonary insufficiency, 1.

If we investigate the frequency with which valvular disease of the heart is complicated by pulmonary tuberculosis we find a number of statistics the import of which lead to similar conclusions. Otto[43] has especially investigated the relation of sex in relation to the present question, and states that tuberculosis of the lungs is more often engrafted upon women suffering from valvular disease than is the case in men. The preponderence of mitral lesions is again evident in the following tabulation:

AUTOPSY STATISTICS IN CASES OF VALVULAR HEART DISEASE.

Author.	Autopsies on heart cases.	No. with pulmonary tuberculosis.	Mitral.			Aortic.			
			Insufficiency.	Stenosis.	Both.	Insufficiency.	Stenosis.	Both.	
Frommolt,	277	22	8	3	1	7	3	...	Aortic stenosis and tricuspid insufficiency 1.
Otto,	48 (in men).	0	22	2	2	4	1	0	Combined lesions, 17.
Otto,	63 (in women).	4	27	10	13	3	2	1	Combined lesions, 11.
Norris,	57	...	8	0	2	8	0	2	

* Personal communication.

CLINICAL REPORTS ON CASES OF VALVULAR HEART DISEASE.

Author.	No. heart cases.	No. pulmonary tuberculosis.	Per cent.	Mitral.			Aortic.			
				Insufficiency.	Stenosis.	Both.	Insufficiency.	Stenosis.	Both.	
Meisenburg,	760	53	7.0							
Eyman,	4138	69	1.7							
Germain See,	277	22	8.0							
Walsham,	91	3	...	...	91					
Schultze,	484	109	22.5	...	...	...	...	...	...	Mitral 4.76 %, aortic 15.4 %, tricuspid 12.8 %, pulmonary 83.3 %; had tuberculosis.
v. Kryger,	59	10	16.9	4	1	0	5	0	1	All ten healed tuberculosis.
Birch-Hirschfeld,	107	5	4.6	...	...	...	...	...	...	2 cases pulmonary stenosis; found 20.8 % tuberculous lesions in individuals without heart disease.
Gillespie,[106]	2368	49	2.06	14	9	6	7	...	3	Tricuspid, 1.

Unfortunately the majority of available statistics, including my own, which deal with the occurrence of recent endocarditis in pulmonary tuberculosis, give no information regarding the microscopic findings or bacteriological examinations. The frequency with which this condition is encountered is shown in the appended tabulation:

	Tuberculous autopsies.	Recent endocarditis.	Per cent.
Teissier	100	32	32.0
Schultze	6937	67	0.966
Osler[42]	216	12	5.5
Kidd	500	6	1.2
Norris	1764	16	0.9
Fenwick	1560	13	0.7
Otto	185	4	3.1
Dittrich[113]	403	1	0.24

Doubtless in the majority of the above cases the acute endocarditis was due to other causes than the tubercle bacillus. In one of Osler's cases fresh tubercles were found upon the mitral leaflet, but no tubercle bacilli could be demonstrated in the sections. Kidd and Councilman also failed to find them. Even when the bacilli can be demonstrated, it is perfectly possible that their presence was simply accidental, as a roughened endocardium would present a favorable ground for the lodgement of micro-organisms carried thence by the blood stream. Lancereaux,[57] Letulle,[58] Perroud,[59] Traube,[60] Fenwick,[61] and others have reported cases of tuberculous endocarditis, but inasmuch as bacteriological evidence is lacking their identity cannot be proved. Anders,[62] who has written an excellent article on the subject, states that these cases are often "associated with other forms of cardiac tuberculosis, especially the pericarditic."

Simple sclerotic endocarditis is met with very commonly in pulmonary tuberculosis, and is presumably due to the toxæmia which is present in the chronic variety of this disease. The researches of Auclair[63] have shown that the metabolic products of the tubercle bacillus possess sclerogenetic as well as necrogenetic properties, which would readily account for the endocardial thickening. Boinet and Romary's[64] experiments have proved that bacterial toxin, even in the absence of bacteria themselves, and without the addition of trauma, are capable of producing changes in the endocardium and aorta. "Ectasine," the vasodilatory substance which Bouchard has shown to be a constituent of the tuberculous toxin by producing vascular relaxation would favor diapedesis of the leukocytes, thus paving the way for sclerogenous processes.

Teissier has enunciated the belief that mitral stenosis is frequently produced by the prolonged action of the tuberculous toxin upon the endocardium, which in time results in a narrowing of the valvular orifice, and states that this form of valvular lesion exerts an inhibitory effect upon the pulmonary disease. If such an inhibition exists, it is more probably due to the increased resistance which the bodily tissues have acquired through the prolonged presence of the toxin in the system than to the mechanical action of the stenosis. Chartier[102] remarks that this sclerogenous tendency is not tuberculosis, but the index of immunity versus tuberculosis.

A tuberculous process may of course be engrafted upon a preexisting valvulitis of different etiology, or the condition may be reversed. Cardiac murmurs occur so frequently in tuberculosis, especially in its later stages, and true tuberculous endocarditis is so rarely encountered, that the condition is hardly ever diagnosticated during life, although this has been done in a few instances. Cases reported as such, in the absence of post-mortem substantiation, have absolutely no value. An interesting case has recently been reported by Debove;[65] an individual, aged thirty-four years, died in a cachectic condition, and at autopsy tubercle bacilli were found in the blood and in the mitral vegetations, no tuberculous lesions being encountered elsewhere. Teissier has classified the various forms of tuberculous endocarditis as follows:

TUBERCULOUS ENDOCARDITIS (bacillary).

a. Granular, discrete or confluent.

b. Caseous.

c. Nodular (vegetative).

ENDOCARDIAL SCLEROSIS (toxic).

a. Generalized.

b. Localized.

Heller,[45] Cornil,[46] and Kundrat[47] were among the first to describe tuberculous endocarditis, but the credit of the first definite and accurate report of this condition belongs to Tripier,[48] who, in a case

of miliary tuberculosis, found a small nodule on the anterior leaflet of the mitral valve which showed the characteristic cellular changes upon microscopic examination, as well as the tubercle bacillus itself. Some time afterward v. Leyden[21] reported four similar cases, in one of which the condition was diagnosticated antemortem. Lion,[67] Londe and Petit[66] demonstrated tubercle bacilli in the valvular endocardium, but derived negative results from inoculation experiments. Similar results were obtained by Etienne,[49] de Thiry,[50] Benda,[51] Poncet and Dor,[52] Ferrand and Rathery,[53] Michaelis and Blum,[54] were the first to succeed with inoculation by producing tuberculous endocarditis in rabbits; and finally Braillon and Jousset[56] demonstrated tubercle bacilli in the blood of a man dying of primary tuberculous endocarditis, the only other evidences of this infection having been a few pleural adhesions. Tuberculous endocarditis usually assumes a verrucose, but sometimes an ulcerative form. According to Benda, the majority of these cases have their origin in a miliary infection, which happens to become localized upon the valves, being in this respect analogous to the condition described by this author as tuberculous endangeitis. In searching through the records of the Philadelphia Hospital two cases were found which were designated as "tuberculous endocarditis;" small tubercles had been found upon the valves, but apparently no microscopic examination had been made.

Vaquez[68] reports a case with very slight pulmonary involvement which developed the signs of an acute mitral endocarditis with cardiac dilatation, the patient rapidly succumbing with evidences of œdema of the lungs. Post-mortem examination of the heart showed a recent marginal mitral endocarditis, in the verrucose structure of which tubercle bacilli were demonstrated. In Ferrand and Rathery's case primary tuberculosis of the spleen was complicated by endocarditis, tubercle bacilli being found in the heart clots and the valvular vegetations. The mode of infection in these cases, the valves themselves having few or no bloodvessels, is probably derived from the heart's blood; lymphogenous infection is of course also possible. The cardiac enfeeblement which occurs in the later stages of tuberculosis would favor the deposition of fibrin upon the endocardium, in which tubercle bacilli could be readily enmeshed. Some cases are due to direct extension of the process from a tuberculous myocarditis. It is much to be desired that microscopic examinations be made of all valvular abnormalities occurring in individuals who show tuberculous lesions in any part of the body.

The effect of valvular lesions upon the course and curability of pulmonary tuberculosis is an interesting one. Some authors, among whom Graham[55] may be mentioned, state that the presence of the former condition, especially when mitral insufficiency exists, and is accompanied by good compensation, exerts a favorable influence

upon the pulmonary disease. von Kryger's 1100 autopsies showed 59 cases of valvular lesions associated with a healed tuberculosis of the lungs. Among 1606 autopsies at the Philadelphia Hospital I found 145 cases of healed pulmonary tuberculosis, 73 of which were associated with abnormal hearts; 35 of these being valvular lesions, and 38 showing well-marked hypertrophy, in the majority of instances due to arteriosclerosis or nephritis. Of the former 27 affected the mitral, 25 the aortic, and 2 the tricuspid valves. Two cases were described as "healing tuberculosis," in one of which a double mitral lesion was present, in the other "chronic endocarditis of the mitral and aortic valves." It is necessary to state, however, that in many of the foregoing cases there was no positive evidence of impaired valve action; a number of them having been simply designated as "chronic endocarditis," "aortic sclerosis," etc. Aneurysm of the aorta was found eight times in 1764 tuberculous autopsies, in one instance it was associated with a healed process. It will be remembered that this is one of the conditions which Rokitansky believed to have an immunizing effect. Fuller[69] states that about 7 per cent. of all cases of aortic aneurysm show evidences of pulmonary tuberculosis; the Brompton Hospital reports show that 7 out of 24 cases of aneurysm were complicated by tuberculosis. Lebert's statistics show this condition in 6 per cent. of the cases. The question as to whether the heart lesion preceded or followed the pulmonary tuberculosis has in quite a large number of instances been carefully determined. In 11 out of 27 cases Kidd[37] found that the heart disease had been first established. Meisenburg[27] reported 49 cases in which a similar state of affairs had existed; in none of these, however, was mitral stenosis present. Duchamp[94] has reported a case of a girl who at the age of eight had chorea, with endocarditis, who suffered from valvular incompetency for years, finally dying at the age of twenty-two of pulmonary tuberculosis. Lannois[95] has recorded an instance in which an individual who had had four attacks of rheumatic fever which resulted in producing both mitral and aortic insufficiency, developed and died of an acute tuberculosis of the lungs. Brousse and Duchamp[96] have noted the occurrence of pulmonary tuberculosis in a girl who had shown the symptoms and signs of mitral insufficiency for years. Otto,[43] after a careful study of the clinical and pathological records of Eichhorst's clinic, covering a period of eleven years, found the coincident presence of pulmonary tuberculosis and heart disease in 6.3 per cent. of the women, but failed to find any such instances among the men. She therefore concludes that the simultaneous occurrence of the two lesions is by no means incompatible, and that malnutrition of the cardiac muscle and insufficient compensatory hypertrophy are conditions which render a tubercular infection more readily possibly. Schultze[25] found antecedent cardiac disease 42 times in 109 cases of pulmonary

tuberculosis, and similar experiences might be quoted almost indefinitely.

When tubercle bacilli enter the blood stream, which they may do either through the pulmonary veins or by direct transmigration from a neighboring focus, they may gain a foothold upon some localized area of the intima, producing either superficial tubercles, infiltration, total occlusion of the vessel, or ulceration, in which case aneurysmal dilatation of the vessel may occur. The latter incidence has been observed in a canine case reported by Hektoen.[70] Cardiac thrombi are a common autopsy finding in pulmonary tuberculosis; Warthin[71] found them in 10 per cent. of his cases; the only case in which a microscopic examination of the clot was made revealed the presence in the basal layers of "epithelioidal tissue containing numerous giant cells, and showing a beginning caseation," red blood cells, fibrin, and tubercle bacilli were also demonstrated. The latter have been found in cardiac thrombi by Weichselbaum,[72] Klebs,[73] Birch-Hirschfeld,[74] Kotlar,[75] Chiari.[76]

Tuberculosis of the aorta occurred only once in the present series of cases. The anterior surface of the vessel underlying the pericardium showed two projecting caseous nodules about the size of a split pea, surrounded by an inflammatory zone, the primary seat of the infection having apparently been in the lungs.

Within the last year Simmitsky[77] has reported two instances of this condition, and collected eighteen from the literature, in which collection are included the cases which are incorporated in Blumer's[78] paper some years before. Tuberculosis of the aorta may arise in four ways: first, by the direct extension of a tuberculous process outside the vessel walls; second, and most commonly, by the deposition of tubercles upon the intima, in which process the other two vascular coats may be but are usually not involved; third, by the infection travelling through the vasa vasorum, the latter case being rather rare, as is shown by the infrequency with which the media has been found to be the seat of disease; fourth, by lymphatic infection, although this necessitates the assumption of an invasion in the opposite direction to the current. As has already been pointed out, the dislodgement of tuberculous thrombi may produce an endangeitis. In a case reported by Kamen,[79] a tuberculous gland which had become adherent to the aorta ruptured into that vessel; as a rule, however, the condition occurs as part of a general miliary invasion. Simmitsky's investigations showed two such cases occurring in 135 instances of the last-named process. From the evidence thus far obtained one is led to believe that arterial lesions such as atheroma or calcareous degeneration, while favoring the deposition of tubercles upon the intima, are by no means a requisite for their production.

Tuberculosis of the myocardium was mentioned by Laennec[111] in 1826; but the first case on record is that reported by Townsend[80]

in 1832. Since then the condition has been studied by numerous observers, among whom may be mentioned Saenger,[81] Pollak,[82] Valentin,[83] Mendez,[84] Labbé,[85] and Anders;[86] in the excellent paper of the latter will be found an extended bibliographical list of authors antedating 1902.

Myocardial tuberculosis manifests itself in four ways:

1. *Large Tubercles.* These may be single or may result from the conglomeration of smaller tuberculous foci. They vary from a small pea to a hen's egg in size. These nodules have a caseous centre and may very closely simulate gummata, a fact which has been attested by Virchow himself.

2. *Diffuse Tubercular Infiltration.* This, the rarest variety, is usually seen in those cases in which the myocardium has become involved as the result of direct extension from the pericardium, the muscular tissue being to a considerable degree destroyed.

3. *Miliary Tubercles.* In these cases the usual miliary tubercles are found underlying but, as a rule, not involving the endocardium, on account of which they are easily overlooked.

4. *Fibroid Tuberculous Myocarditis.* The existence of this form was for some time questioned inasmuch as Brehmer's[87] case was the only one on record. Since then, however, a similar case has been described by Gandy,[89] and a definite identity established. The pathological findings in these cases consist of diffuse infiltration of round cells and connective tissue. Microscopically, giant cells, caseous areas, but no tubercle bacilli have been demonstrated. This variety of myocarditis is presumably due to toxæmia, being comparable to tuberculous cirrhosis of the liver and similar to the muscular sclerosis found in the horse by Cadiot, Gilbert, and Roger,[88] as well as the muscular fibrosis of chronic tuberculosis described by Klippel.

Nearly half of the reported cases of tuberculous myocarditis occur in individuals under fifteen years of age, no especial predilection for sex having been noted. The majority of the cases seem to owe their origin to infection of the pericardium; the endocardium, on the other hand, does not often seem to share in the extension of the disease. The following table shows the frequency with which the condition has been encountered.

			Per cent.
Rokitansky	116	2	1.7
Louis	112	0	0
Willigk	1825	2	0.1
Valentin[83]	3203	7	0.21
Chambers	566	2	0.3
Sangali[90]	796	2	0.2
Fuchs[91]	285	1	0.4
Dittrich	403	1	0.28
Norris	1764	5	0.28

Stephani[92] has during the past year collected and tabulated most of the reported cases of large conglomerate heart tubercles

from the literature and found but 36. Localized areas of myocardial tuberculosis as an accompaniment of tuberculous pericarditis is quite a frequent autopsy finding, but large caseous masses are a considerable rarity. Kaufmann,[97] in his *Pathological Anatomy*, states that he has seen a tuberculous mass the size of a goose egg involving the wall of the right auricle.

The source of infection in myocardial tuberculosis, in the same manner as when the pericardium is thus involved, is usually from the bronchial or mediastinal glands. The frequency with which these structures are the seat of an active or latent tuberculosis has been pointed out in another paper.[93] Cabannes[98] has written an article upon tuberculosis of the auricles in which he calls attention to the enormous size of the tubercles which have been found infiltrating these structures; according to the last named author these cases owe their origin to infection from the adjacent lymphatic glands. Primary tuberculosis of the myocardium has been described by Demme,[99] Noel,[101] and Knopf, but the existence of such a condition has not been generally accredited. In 1764 tuberculous autopsies I was able to find tuberculous myocarditis six times. In one case small miliary tubercles were found scattered through the muscle fibres in a case of acute general infection; the other cases were associated with tuberculosis of the pericardium; none of the cases showed large caseous masses. Microscopic examinations of the cardiac muscle were recorded in 41 tuberculous cases at the Pennsylvania Hospital with the following results:

Normal muscle	14
Chronic interstitial myocarditis	10
Parenchymatous degeneration	9
Fatty degeneration	5
Brown atrophy	3

Cultures were made from the heart's blood in 21 cases of pulmonary tuberculosis, resulting as follows:

Sterile	14
Micrococcus lanceolatus	3
Staphylococcus pyogenes aureus	1
Streptococcus mucosus	1
Micrococcus citreus	1
Bacillus alkigenes	1

The foregoing results tend to substantiate the observations of clinical experience. In the wards of the Phipps Institute, where a considerable number of patients with advanced pulmonary tuberculosis are assembled, it has frequently been observed that after remaining in a stationary condition for a considerable length of time, five or six individuals will often die in rapid succession and without very evident cause, suggesting the fact that this sudden rise in the mortality rate has been due to an acute infection which had gone the rounds of the ward.

Tuberculous myocarditis may be closely simulated by gumma, carcinoma, and actinomycosis. The first of these is to be distinguished from tuberculosis by being more sharply circumscribed from the surrounding tissue, when microscopically examined, and also by being grayer in color. Carcinoma contains less moisture, and is more brittle. Actinomycosis may be impossible of differentiation, unless tubercle bacilli or hooklets are found.

CONCLUSIONS. 1. In view of the frequency with which tuberculosis of the lungs has been found to be associated with valvular heart disease, we are forced to conclude that the latter exerts, if any, but very slight influence upon the former, either as an inhibitive or curative influence, even if satisfactory compensation is maintained. On considering the relative frequency of valvular lesions in general, mitral stenosis does not seem to be less often coincident with tuberculous disease of the lungs than other varieties of heart lesion.

2. It is doubtful whether smallness of the heart predisposes to pulmonary tuberculosis of the lungs to a greater degree than is explainable by the general systemic underdevelopment and lack of resistance which such individuals often exhibit. It is a fact, however, that small hearts, either as the result of wasting or hypoplasia, are commonly found at tuberculous autopsies, while large hearts are not often encountered in uncomplicated cases.

3. Stenosis of the pulmonary orifice seems to favor the development of tuberculosis of the lungs. A very large proportion of these cases die of the latter disease.

4. Arterial and endocardial thickening is a common result of tuberculous intoxication, but it is doubtful whether this process attains a sufficient degree to produce valvular incompetency, as claimed by Teissier.

5. Tuberculous endocarditis and myocarditis, particularly the former, occur with considerable rarity, but pericarditis, especially the chronic forms, very frequently owe its existence to the presence of the tubercle bacillus.

6. Tuberculosis of the aorta is also a finding of considerable rarity; the condition may result in the formation of an aneurysm.

7. The cardiac muscle undergoes various forms of degeneration in pulmonary tuberculosis, fatty and fibroid changes being very common, a fact which explains the signal failure of digitalis and certain other heart stimulants to benefit these cases.

8. Uncomplicated cases of pulmonary tuberculosis often exhibit such striking differences in resistive power and frequently evince such a remarkable tendency toward recovery, even in seemingly hopeless cases, that we should accept only the most absolute evidence as a proof that either the coincidence of another pathological condition or the administration of a special remedy has conferred a benefit upon the patient.

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CONCERNING HÆMAGGLUTININS OF BACTERIAL ORIGIN AND THEIR RELATION TO HYALINE THROMBI AND LIVER NECROSES.*

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Elsewhere one of us[1] has described the hæmagglutinative power of various cytolytic immune sera and the relation of the red blood corpuscle thrombi (hyaline thrombi) resulting from the injection of such sera to focal hyaline necroses of the liver. The distinct character of the liver lesions thus produced and the fact that they could be explained only by the presence of agglutinated red blood corpuscle thrombi suggested the possibility that similar lesions occurring in various infectious diseases might be due to the development of hæmagglutinins of bacterial origin. In order to test this supposition we have attempted to demonstrate the presence of hæmagglutinins in filtrates of bacteria treated in various ways and by the injection of the same into animals to produce agglutinated red blood corpuscle thrombi and associated liver necroses.

It is not our intention to go into the general literature of these subjects, but merely to touch upon those points which relate to infectious conditions. The more important views concerning liver necroses may be found in the papers of Flexner,[2] Mallory,[3] Boxmeyer,[4] and Opie.[5] That the so-called hyaline thrombi may be composed of altered and fused red blood corpuscles, we consider to be definitely established. The recent studies of Flexner,[6] Boxmeyer and Pearce offer conclusive evidence of such origin, and support the earlier observations of Klebs[7] and Ziegler.[8] The occurrence of hyaline thrombi in connection with various infectious and toxic conditions has been emphasized by Welch,[9] who, in his summary of the literature mentions particularly infections with S. pyogenes aureus and B. choleræ suis, and offers a suggestion concerning their origin from red blood corpuscles. In a later discussion[10] of the subject he brings forth the hitherto unpublished observation of Fisher concerning the plugging of small vessels by agglutinated red cells, as the result of injecting typhoid bacilli, and calls attention to the evidence in favor of the interpretation of many of the hyaline thrombi

* This study has been conducted under a grant from the Rockefeller Institute for Medical Research.

as derived from fused red blood corpuscles. Other important observations are those of Flexner, who found similar thrombi in the intestine of typhoid fever, in bronchopneumonia, and in experimental diphtheria; and also of Boxmeyer who could distinguish, in the livers of rabbits dying of experimental hog cholera, between necroses due to endothelial cell thrombi and those due to agglutinated red blood corpuscle thrombi. The hyaline thrombi occurring in various intoxications due to either organic or inorganic poisons, and in toxic conditions of doubtful origin, as eclampsia, are undoubtedly of similar nature; but as they do not come within the scope of this paper, will not be further considered.

Of considerable historical interest, in connection with this question of the occurrence of red corpuscle thrombi in the course of infectious diseases are the observations of Hueter,[11] made in 1873. As the results of his studies, to which attention has recently been called by Welch,[10] Hueter came to the conclusion that clumping of red blood corpuscles causing permanent or transient occlusion of capillaries and small vessels ("globulöse Stase und Embolie") occurred not uncommonly in septic and other fevers. His theory that this phenomenon constituted the underlying basis of fever has never gained acceptance, but the observations are of interest in connection with our recently acquired knowledge of bacterial hæmagglutinins. v. Recklinghausen[12] considers this globular stasis of Hueter to be analogous to a condition found in the capillaries after transfusion of alien blood, and which he described as an "agglutination" of red blood cells.

In planning this investigation it was evident that as necroses of the liver are most frequently associated with infections by the bacillus of typhoid fever and the bacillus of hog cholera, the bulk of the work should be done with these organisms. In order, however, that no opportunity might be lost, the literature dealing with bacterial hæmolysins was examined in the hope of finding references to organisms which produced also hæmagglutinins. Of twenty-nine such investigations,[13] but six[14] refer to the production of hæmagglutinins by bacteria. Kraus and Ludwig found that bouillon cultures of S. pyogenes aureus and Vibro Paris had the power of agglutinating red blood corpuscles, *in vitro*, in from ten to twenty-four hours at room temperature. The mass which settled at the bottom of the tube was seen upon agitation to be composed of small clumps of red blood corpuscles which could not easily be disintegrated. The agglutinin they considered to be independent of the hæmolysin; but, on the other hand, they state that organisms which do not hæmolyze also do not agglutinate. Small amounts of the cultures caused agglutination without hæmolysis. Volk and Lipschütz, working with staphylolysin and vibriolysin, describe agglutination in connection with incomplete hæmolysis of rabbits' blood, but did not observe it with other bloods. Volk, as a result of his

observations, comes to the conclusion that agglutination is due not to a specific body, but to non-isotonicity of the fluid. Calamida states that no agglutination precedes the hæmolysis caused by bouillon cultures of the chicken-cholera bacillus. Flexner mentions agglutinins of low activity in filtrates of B. pyocyaneus, B. typhosus, and S. pyogenes aureus. Kayser, in his study of colilysin, observed a clumping of red cells in connection with incomplete hæmolysis, but not when complete solution occurred. Of greatest interest, however, and very suggestive, is the observation of Eisenberg,[15] who found the blood of an individual with a generalized pyocyaneus infection to be both autoagglutinative and isoagglutinative.

As the result of this survey it seemed advisable to utilize B. pyocyaneus and S. pyogenes aureus in addition to B. typhosus and B. choleræ suis; and these with B. dysenteriæ and S. pyogenes constituted the group of organisms finally selected for study.

METHODS. In previous attempts (Reed,[16] Flexner, Mallory and Boxmeyer) to produce liver necroses by the injections of micro-organisms, either the living culture grown in the ordinary way or its filtrate has been used. With the use of the former it has been difficult to distinguish between the direct action of the organism and the effect produced by its toxin; with the latter the action of intracellular toxins has been excluded. In our experiments the direct action of the micro-organisms has been eliminated by the use of filtered fluids, and an attempt has been made to obtain the intracellular constituents of the bacterial cells by the utilization of methods destined to cause its disintegration. Various writers have described methods by which the bacterial cell is destroyed and its receptors liberated. Of these methods we have tried, with certain modifications, the processes of autolysis described by Conradi,[17] Neisser[18] and Shiga, and Brieger and Mayer.[19] The various organisms have been grown for twenty-four to seventy-two hours on agar in large flat flasks having a surface of 20 x 8 cm. The growth on several flasks, usually three or four, has then been scraped off, subjected to 55° C. for forty-five minutes, and placed in tubes containing 0.85 per cent. salt solution at a temperature of 37.5° C. for two to three days. In some instances the fluid has stood for longer periods, varying from one to seven weeks. The fluid has then been filtered (Chamberland B. and F.) and injected intravenously into animals, after testing its agglutinative power *in vitro*. At various stages of the process suitable controls were made to demonstrate absence of contamination and the efficiency of the filters.

In addition to this method of growing the organism, an attempt was made also to stimulate the production of hæmagglutinin by previously growing the organisms in media containing red blood cells. This method was suggested by the theory of "bacteriogenic cytotoxins" advanced by Welch in his Huxley Lecture: "Certain

substances of the host of cellular origin, assimilated by the parasites through the possession of haptophore groups with the proper affinities, become anchored to receptors of the parasitic cell, which, if not too much damaged, is thereby stimulated to the overproduction of like receptors; these excessive receptors of the parasite, if cast off into the fluids or the cells of the host, then constitute intermediary bodies," etc. The writer further states "by a similar mechanism it is possible that parasites may be stimulated to the production also of antibodies other than cytotoxins, such as various agglutinins, precipitins, antienzymes—all adjusted against the host."

Assuming that if this hypothesis might apply to organisms growing in living cells or fluids, it might hold also for those grown on cells outside the body; typhoid and hog-cholera bacilli have been grown in various blood preparations. These include both defibrinated and washed blood added in various proportions to salt solution and fresh sterile rabbits' organs. The period of growth in the various blood mixtures varied from twenty-four to seventy-two hours; in some instances inoculations into fresh blood solutions or upon fresh organs being made on each of three successive days. The sterile organs were prepared according to the technique described by Flexner.[20] By these various methods it was hoped that the organism would be stimulated to produce agglutinins, and that this power would be retained during the subsequent growth on agar, giving in the finished autolyzed product a fluid of appreciably augmented agglutinating power. Observations supporting this theory have been made by Marmorek and by Simon, who found that streptococci grown in media composed of leukocytes alone, or with bouillon added, secrete a toxin of considerable power. Simon[21] believes that the streptococcus in order to secrete toxin must meet a certain resistance to its development, and that this resistance is furnished by something in the leukocytes. This explanation, put in the terms of Ehrlich, corresponds to Welch's hypothesis. Our attempts to produce free agglutinin receptors by growing the organisms in blood we consider analogous to Simon's method of producing toxin by growth in leukocytes.*

Another method employed was the growth of an organism in heated rabbit serum. This was suggested by the observation of Besredka[22] that the streptococcus produces an hæmolysin when thus grown.

Results. The tests for agglutination were made by adding nine parts of the various filtrates to one part of blood. Obser-

* Another point in favor of this theory of bacteriogenic antibodies is the observation of Theobald Smith (verbal communication) that recently isolated cultures of the hog-cholera bacillus have a greater power to produce liver necroses than have old cultures. Accepting Boxmeyer's work on the relation of agglutinative red blood corpuscle thrombi to such lesions the explanation naturally suggested is that residence in the animal has stimulated the power of the bacillus to produce agglutinin.

vations were made at room temperature and at 37.5° C. at varying periods up to twenty-four hours. The clumping of red blood corpuscles by bacterial hæmagglutinins is of slight degree as compared with that produced by various cytolytic immune sera. The powerful agglutination of the latter is never seen, and for this reason more careful comparisons with controls is necessary in order to detect slight differences in reaction. This feeble activity renders it difficult to make definite statements concerning some of the organisms studied. While all (B. typhosus, B. choleræ suis, B. pyocyaneus, B. dysenteriæ, S. pyogenes aureus, and S. pyogenes) in the majority of tests *in vitro* showed a slight agglutination as compared with controls, the effect of filtrates of B. dysenteriæ, B. choleræ suis, and B. pyocyaneus was so slight as to be considered doubtful. With other organisms the agglutination was more evident, being most distinct with filtrates of S. pyogenes. Upon microscopic examination (hanging drop) the clumping caused by the streptococcus was always in the form of massive, more or less branching, rouleaux; while with all other cultures an irregular agglutination of a small number of corpuscles was seen. The agglutination due to the streptococcus could be seen after fifteen to twenty minutes as the corpuscles settled; while with the other organisms it could be seen only upon agitation after a considerable period of time. More definite results were obtained with rabbits' blood than with dogs' blood.

Of unusual interest and very suggestive are the agglutination tests with filtrates of typhoid bacilli previously grown in blood suspensions and on fresh sterile organs; though carried out in but a small number of tests they appear to be confirmatory of Welch's hypothesis mentioned above. These filtrates, especially those of bacilli grown on sterile organs, exhibit an appreciably greater power of agglutination than the filtrates of organisms grown on agar only.

While no effort was made to study especially bacterial hæmolysins, it is of interest that the autolytic products of bacteria as here prepared have never caused hæmolysis. This result is in harmony with the observations of Jordan,[23] Williamson,[24] and others, who hold that the hæmolysis produced by some bacterial filtrates (B. typhosus, B. pyocyaneus) is to be explained by the presence of an alkali elaborated in the growth of the organism. The filtrates used in our tests have all been faintly acid to phenolphthalein.

The animals selected for the injection experiments were dogs and rabbits, the former receiving 5 to 20 c.c. (dose, 1 : 1514 to 1 : 235) of the filtrates in either the saphenous or mesenteric vein; the latter 1 to 20 c.c. (dose, 1 : 1790 to 1 : 64) in either mesenteric or marginal ear vein. In all, twenty-nine injections have been made; in no instance did death occur as the immediate result of the injection. Necroses of the liver occurred in ten of the animals. Two of these we have thought best to exclude, because of associated coccidiosis,

although the necroses appeared to be entirely independent of the parasitic invasion; another has been excluded because of the chronic character of the lesion. The remaining seven cases exhibited typical necroses, two occurring in dogs and five in rabbits. These lesions followed the injection of filtrates of the typhoid bacillus in three cases, of the hog-cholera bacillus in three cases, and of the dysentery bacillus in one case. Filtrates of the B. pyocyaneus, S. pyogenes aureus, and S. pyogenes did not cause necroses. These necroses are not always visible to the naked eye, but when seen macroscopically they appear as miliary points, or occasionally as round or oval areas or linear streaks of grayish color and distinctly separated from the normal liver tissue. They are very few in number compared to those produced by the agglutinins of cytolytic immune sera, and are usually limited to the superficial portions of the liver lobes. Portions of the liver in contact with other lobes or adjacent organs are more frequently involved than the free surfaces. Histologically, the liver cells exhibit a hyaline necrosis, the nuclei being entirely destroyed or evident merely as faint rings; fragmented or pyknotic nuclei were seldom seen. In many of these areas the vessels are filled with red blood corpuscles, more or less altered and fused, and suggestive of hyaline thrombi. This condition, however, is not constant, and is not so evident as in the necrotic lesions produced by cytolytic immune sera. On the other hand, larger vessels, especially the smaller branches of the portal vein, contain typical agglutinative red corpuscle thrombi more or less completely occluding the vessel. Similar thrombi of small vessels have been seen in other organs, as the kidney, spleen, and lymph nodes, but without definitely associated lesions. Other thrombi, as those composed of endothelial cells, fibrin, etc., have not been seen in the liver.

Fatty changes in the liver and kidney, intense congestion of the spleen and lymph nodes, and a proliferation of the endothelial cells of the lymph sinuses have been found not infrequently after the injection of typhoid and hog-cholera filtrates. A relation between these lesions and the injected fluids cannot, however, be readily demonstrated; the proliferation of endothelial cells, especially, is not infrequent in apparently normal animals. That some injury to the kidney is brought about is indicated by the appearance of albumin in the urine after the injection of filtrates of B. typhosus and B. dysenteriæ.

The results of the injection of filtrates of typhoid and hog-cholera bacilli grown upon blood media, while very suggestive, are not conclusive, owing to the small number of observations. But six filtrates so grown were injected. Filtrates of the typhoid bacillus grown in blood suspensions, while possessing an increased agglutinating power *in vitro*, did not cause necroses upon injection; on the other hand, two different filtrates of the same culture grown for several

days on sterile rabbits' organs caused the most extensive lesions observed in the course of this investigation. The bacillus of hog-cholera grown in blood suspensions caused, in one instance, lesions in the liver. The attempt to produce necroses with such filtrates has therefore been successful in three of six experiments, while with filtrates of the same organism grown on plain agar, necroses resulted in three of twelve attempts. These results are suggestive in connection with the increased agglutinating power observed *in vitro*, but the small number of experiments does not warrant definite conclusions.

Filtrates of B. typhosus grown in heated rabbit serum produced no lesions upon injection into rabbits.

Conclusions. The filtered autolyzed products of a number of bacteria possess hæmagglutinins of low activity, the formation of which may be stimulated by previously growing the micro-organisms on media containing fresh red blood cells. The injection of these filtrates into dogs and rabbits is followed in some instances by the occurrence of liver necroses with associated fused red blood corpuscle thrombi; like thrombi may occur in other organs. These thrombi are similar in structure to those generally described as hyaline thrombi. The demonstration of agglutination *in vitro* and the association of the fused red cells with the liver lesions suggest a relation of the agglutinin to the lesions. This relation, however, cannot be considered as proven, for it is impossible to exclude the effect of toxins acting directly upon the liver cells; on the other hand, the similarity of the lesion to the very definite necroses caused by the powerful agglutinin of cytolytic immune sera strongly supports the possibility of such a relation.

The results observed by us are in accord with the slight potency of the agglutinin obtained. It is probable that methods which cause a more complete disintegration of the bacterial cells, as those employed by Vaughan,[25] and by MacFadyan and Rowland,[26] would yield an agglutinin as powerful, comparatively, as the toxins so derived, and capable of producing lesions more analogous to those caused by the agglutinins of cytolytic immune sera.

We present this communication, therefore, not as an attempt to prove that all hyaline thrombi are composed of fused red blood corpuscles or that all liver necroses are caused by such thrombi, but rather to indicate the evidence in favor of the view that these lesions, in some instances, may be due to bacterial hæmagglutinins.

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I. REPORT OF AN ANOMALOUS LATERAL SINUS. II. REPORT OF A CASE OF THROMBOSIS OF THE LATERAL SINUS.

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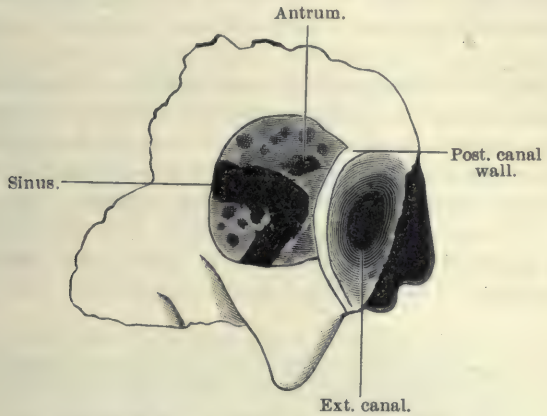
The first case is put on record because of the anatomical anomaly presented in the course of the lateral and sigmoid sinus. The patient was admitted to St. Mary's Hospital in an extremely low condition, and operated upon for cerebral abscess, but the condition grew steadily worse, and the patient died twelve hours after operation. No autopsy was permitted, and consequently a full description of the anomaly cannot be given. The accompanying illustration will show the course taken by the sinus. It lay immediately beneath

the external table and passed *through* the mastoid cells, being surrounded an all sides by pus, granulations, and mastoid cells. It looked exactly like a large tube passing through the mastoid space.

The horizontal portion crossed the mastoid space entirely, being separated from the external canal by a layer of bone not more than



Case I., showing passage of sinus across mastoid space.

3 mm. in thickness, and then made a sharp bend down and backward. It passed just below and external to the antrum instead of being on a level with it. It is to be much regretted that no autopsy was permitted, as it would have been very interesting to follow the complete course of the vessel.

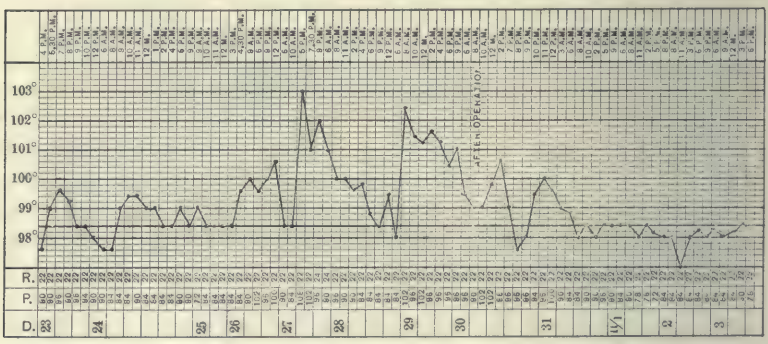
The second case is one of thrombosis of the lateral and sigmoid sinus. Mrs. K. S., aged twenty-three years, had most of the diseases of childhood, except scarlet fever. When a child she frequently had earache, but there is no definite history of a discharge. Present trouble began in October, 1903, when she complained of pain all over the head, tinnitus, vertigo, anorexia, and discharge from the right ear. The patient received careful treatment for her condition, but temporary relief only was obtained, and she was sent to St. Mary's Hospital by her physician, Dr. H. L. Picard.

Upon admission the pain was referred to the occiput, the mastoid, and the region behind the angle of the jaw. There was œdema over the mastoid and occiput, with doubtful tenderness along the jugular. The tympanic membrane was red and bulging, and the canal wall red and sagging. The presence of purulent mastoiditis was diagnosed, but, owing to the symptoms, the possibility of sinus thrombosis was considered, and it was decided to delay and keep the patient under close observation. The accompanying chart will show the characteristic temperature. Free paracentesis and incision of the canal wall, hot douching, and dry heat externally,

with calomel internally, was the treatment given and under which the pain was somewhat lessened.

On the fourth day after admission there was a sharp rise in the temperature, but close questioning failed to elicit history of a chill. The temperature fell gradually during the ensuing thirty-six hours, when there was another sharp rise of four degrees, and the patient said she noticed a clammy perspiration. Immediate operation was advised.

The usual tympanomastoid exenteration was done first; the sigmoid sinus was found uncovered and contained a firm clot. The bone was removed in the direction of the jugular bulb and backward along the lateral sinus, the latter also being filled with a clot. It was then deemed best to ligate the jugular vein before going farther. The vein was found to be soft, but the walls above the point of entrance of the facial were gray, and showed signs of clot formation. The vein was ligated about 3 cm. below and 3 cm.



above the facial, the latter was ligated and cut, and the jugular vein excised. The sinus wall was freely incised and a Randall sinus curette passed down toward the jugular bulb and backward through the lateral sinus for about 5 cm. until a free flow was obtained, as much of the clot as possible being removed. At first there was a considerable quantity of an offensive, reddish-brown fluid, and the flow was allowed to continue until the normal dark-blue blood appeared.

The neck wound was closed throughout with interrupted sutures, and the usual sterile dressings applied. On the fifth day following the operation the first dressing showed the neck wound healed by first intention, and the mastoid condition doing well. Convalescence was without complication of any kind, and healing has been perfect.

In most cases given, the œdema over the occiput, tenderness behind the angle of the jaw and over the jugular, operation might have been indicated by the first rise of temperature; but as this was coincident with marked constipation and the temperature fell

following an enema, and as no history of a chill could be obtained, it was thought best to wait.

The features of this and other cases of suspected sinus involvement would seem to clearly indicate that by far the best method of procedure is to open the mastoid early and uncover and carefully examine the sinus, for undoubtedly every hour counts in these cases. This patient, being under observation, was operated upon early enough to protect her from fatal infection; but in some of our cases that are not seen until the advanced stage of infection is reached, delay in intervention could unquestionably be serious or even fatal. In these cases the jugular vein plays a most important part, and decidedly the safest course would seem to be either to tie off the vein or excise as much of the vessel as its condition indicates.

A CASE OF GLIOMA IN THE SELLA TURCICA.[1]

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Following is a case of new-growth in the pituitary region peculiar in producing an intercellular substance which stains like neuroglia. The tumor grew in all directions and notably forward and downward, with partial destruction of the gland and perforation into the sphenoidal sinus. Death occurred six years after onset of symptoms. There were symptoms of heightened intracranial tension, impairment of vision, an unusual kind of ("ear-to-ear") headache, and rhinitis. There was no acromegaly.

Clinical History. Mrs. ——, aged forty-eight years, family history good, previous health good.

History of present illness: Early in 1897 patient noticed slight impairment of vision. In July, 1898, the visual defect grew worse, and slight headaches developed. Dr. Knapp then examined her eyes, with results as follows: Right eye counts fingers eccentrically at 30°; left eye 20/40, with + 1 D. glass 20/30; ophthalmoscope shows right optic atrophy; no other intraocular disease. A second examination by Knapp in April, 1899, showed that right eye could see only movements of the hands; left eye with + 1 D. glass 20/30; there was complete bilateral temporal hemianopsia, and the nasal field

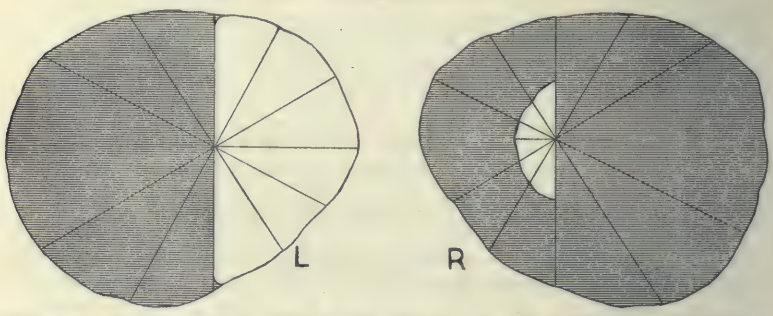
[1] Presented at the Fourth Annual Meeting of the American Association of Pathologists and Bacteriologists, New York City, April 2, 1904.

of right eye was much contracted, extending only 20 degrees toward the nasal side.

In August, 1899, there occurred an attack of coma ushered in by violent headache and nausea. With slight remissions, the attack lasted several days. There were no convulsions. Following this illness mercury inunction and potassium iodide were used, and the patient regained the degree of health possessed before the attack. During the winter (1899–1900) headaches became more frequent; they were often frontal in location, but frequently seemed to transfix the head, passing from ear to ear. Rhinitis developed, and with every exacerbation of the nasal congestion the headache became worse. There was some unsteadiness of gait.

In August, 1900, a briefer attack of coma occurred similar to that of 1899. In January, 1901, a third attack. One of us (F. H. H.) saw the patient in this attack. There was absolute coma, flushed face, slow, full pulse, fever, strabismus. There was and

FIG. 1.



Visual fields, showing bilateral temporal hemianopsia (from the notes of Dr. Herman Knapp two years after the onset of symptoms).

had been no sign of nephritis, neither was there paralysis at any time (except the ophthalmoplegia). There were no convulsions. The attack lasted about one week, during three days of which the patient was comatose.

A fair measure of health was regained after this attack, and maintained for two years. During this time the patient was fairly active, walking on the street daily, though with unsteady gait. There were occasional headaches. On two or three occasions there were transient seizures of violent headache and nausea, but without coma. The visual defect progressed until the right eye was totally blind and vision very defective in left.

In April, 1903, a final attack similar to former ones occurred and terminated in death.

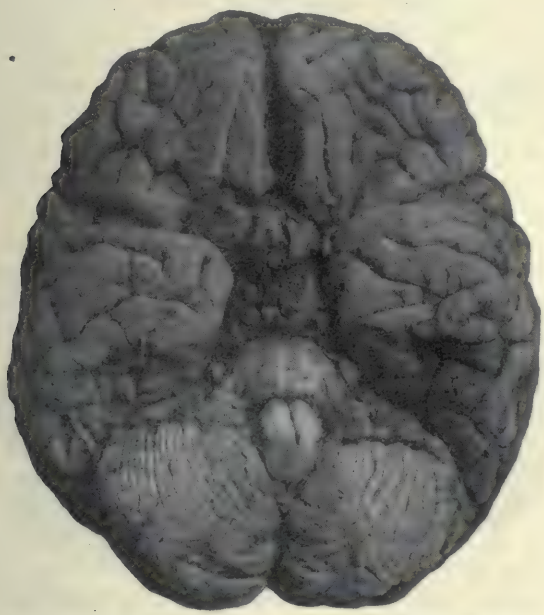
(Dr. E. E. Mather, of Williamstown, physician to the patient, has kindly given us many of the clinical data. Notes of the ophthalmic findings have been kindly furnished by Dr. Hermann

Knapp, of New York. A part of the neurological account is due to Dr. M. Allen Starr, of New York, who saw the patient at various times during her disease.)

Clinical Summary. Symptoms at intervals during six years. Progressive impairment of vision. Frontal and ear-to-ear headache, more severe in attacks of rhinitis. Various seizures with headache and nausea. Attacks of coma forty-four, thirty-two, and twenty-seven months before death. Death in a fourth attack.

Gross Findings. *Necropsy.* Performed twenty hours postmortem. The cranium only was opened.

Fig. 2.



Ventral aspect of brain, showing tumor in interpeduncular space.

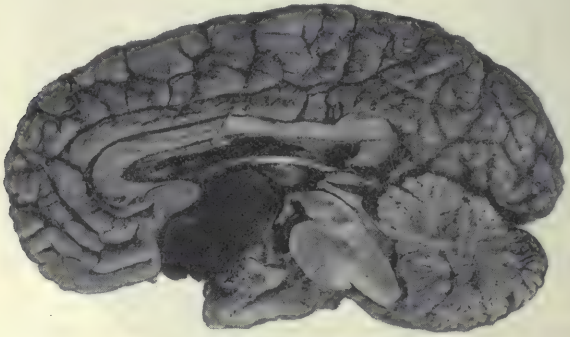
Body well nourished. Physiognomy normal. Calvarium of normal thickness. Pial vessels much engorged. No increase of arachnoid fluid. On raising frontal lobes a mass is seen in the neighborhood of optic chiasm, firmly adherent in places to sella turcica. Floor of sella thinned and broken through in places, opening into the sphenoidal sinuses, which contain pus. From below a conspicuous dark-brown mass is seen to occupy the interpeduncular space and to extend from the pons forward beyond the position of the optic chiasm. (Fig. 2.) The tumor hides all parts of the visual path except the extremity of the divided left optic nerve. Projecting from the tumor anteriorly, dorsally, and laterally into the right frontal lobe is a cyst of hazelnut-size containing a clear blood-

tinged fluid. A mesial section of the brain (Fig. 3) shows that the tumor lies anterior to the corpora albicantia, occupying the position of the pituitary body. The floor of the third ventricle is stretched over the dorsal surface of the tumor, and is melted down in part, so that the tumor projects into the third ventricle, encroaching to some extent upon the anterior portion of cavity. The tumor projects dorsally through cerebral substance into the lateral ventricle. The lateral ventricles are somewhat dilated.

The chiasm and the right optic nerve are totally destroyed. The tumor itself is thinly encapsulated and shells out easily from its bed of cerebral substance, and is of a spongy consistence anteriorly, more compact posteriorly. The spaces of the spongy tissue are filled with cruor clots.

Summary of Gross Findings. Single, compact, in places spongy or hemorrhagic tumor, filling interpeduncular space, producing atrophy of floor of sella turcica, encroaching upon lateral and third ventricles, and effecting atrophy and complete destruction of optic chiasm and right optic nerve, with partial destruction of optic tracts.

FIG. 3.



Mesial aspect of brain.

FINER ANATOMY. Endeavor was made to get at the duration of the process by tracing out roughly the degenerations in the optic apparatus. More evidence was obtained from the tissues of the tumor itself upon the crucial point of the relative age of its different parts.

The microscopic findings follow:

1. The cortex in many places, though not everywhere, exhibits slight neuroglia changes, consisting in a moderate increase of the large neuroglia cells of the subpial layer and an increase (or increased staining capacity) in the fibrillæ in the outermost lamina. We should like to interpret these changes as a response to the universal pressure and consequent flattening which attend new-growth or other swelling in intracranial tissues. Sections from the orbital cortex adjacent to the tumor show the thickest fibrillæ, which are

arranged as a rule tangentially. In general there are more fibrillæ in the sulci than over the tops of the gyri. There is some evidence for maintaining that there are more fibrillæ (without notable increase of cells of origin) opposite the vessels and especially opposite the larger arteries (compare fibrous increase in supra-arterial epicardial nodules). The method of demonstration here used was the phosphotungstic-acid-hæmatein method after formalin fixation and mordanting with picric acid and ammonium bichromate (Mallory).

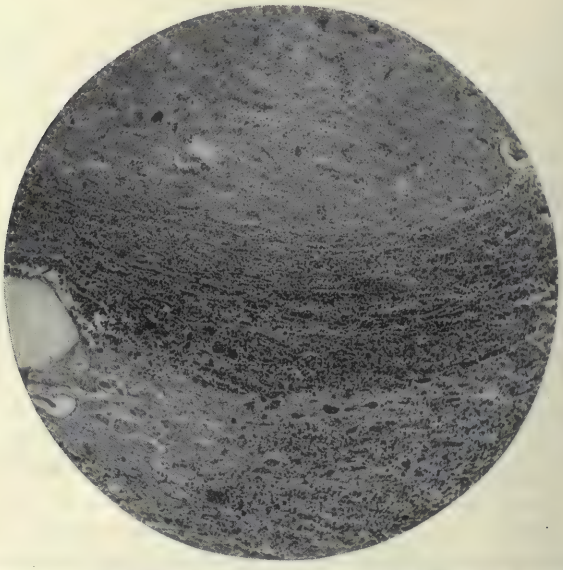
2. Work with the Nissl method (paraffin sections of formalin-fixed material) was negative or unsatisfactory. The adventitial spaces about the smaller vessels are free from exudative cells. Many of the isolated glia cells and some of the satellite cells show numerous coarse grayish-green pigment granules in limited masses serving very well to mark out the glia cell bodies which are not otherwise in evidence. Similar appearances are sometimes shown in Zenker-fixed material of various origin and without other lesion. Many of the nerve cells are moderately pigmented. The nerve-cell picture is unsatisfactory. Many of the nuclei are swollen; some show foldings of the nuclear membrane. The cell layers are demonstrable. The medullary glia shows an orderly arrangement of nuclei.

3. Unmistakable early degeneration is demonstrable by the Marchi method in the left optic nerve (central bundles show the most distinct blackening), in the left lateral geniculate body (dense bundles of degenerate fibres intercalated with normal bundles), in the left anterior quadrigeminal body (stratum zonale shows marked change, many of the sagittal fibres of the nucleus are blackened), and in the lateral geniculate and anterior quadrigeminal bodies on the right (diffuse changes).

Longitudinal sections of the left optic nerve stained by the Weigert method for myelin show almost total loss of staining capacity except in a central core (probably attacked last, as shown by the Marchi method). The lateral geniculate bodies and the anterior quadrigeminal bodies stain well by Weigert; probably all the fibres of the stratum zonale and most of the fibres of the nucleus retain the stain. A small area of undoubted degeneration of some standing was made out by the Weigert method in the left pulvinar; but this was not further traced.

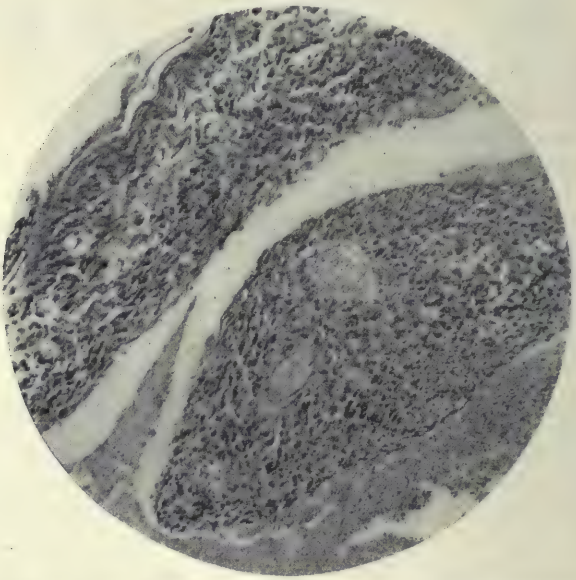
4. Microscopic examination of various portions of the tumor showed, first, some anterior pituitary substance; second, neoplastic tissue adjacent to and compressing the glandular substance. (Fig. 4.) The new formation showed an almost homogeneous structure except in amount of fibrillary intercellular substance. (Fig. 5.) The mass contains numerous well-developed vessels besides numerous thin-walled vessels, many of which have ruptured to form fairly wide lacunæ of blood. The cells are in many places so grouped about the vessels as to suggest the appearance of certain sarcomata of vascular origin.

FIG. 4.



Section showing strands of gland substance of anterior lobe of hypophysis compressed by the tumor. The gland contains numerous masses of colloid. The cytoplasm of the chromophile cells of the gland stains deeply with phosphotungstic-acid-hæmatein. (Mallory.)

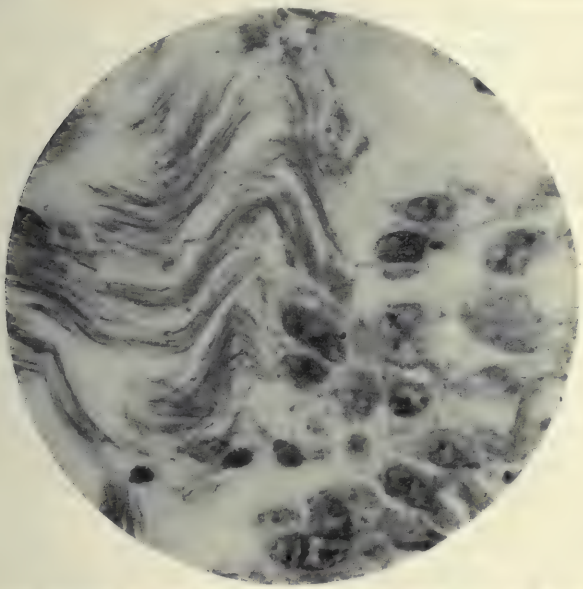
FIG. 5.



Low power view of tumor, showing trabeculæ of cells separated by a space containing blood and coagulated serum. The lower band of cells shows a striate or wavy structure due to the included fibrillæ. Section stained with Mallory's phosphotungstic acid-hæmatein (formol fixation, mordanting with picric acid and ammonium bichromate).

Owing to poor fixation or on some other ground it seemed impossible to prove the tumor a sarcoma by demonstrating an intercellular substance responding to the aniline-blue stain (Mallory). Attention was therefore drawn to a very few scattered fibrillæ taking the acid fuchsin in the aniline-blue method. With a view to making out the nature of these fibrillæ, pieces of the mass from a part adjacent to the bone were mordanted by the picric acid and ammonium bichromate process and stained by phosphotungstic acid hæmatein. By this method numerous bundles of parallel fibrillæ standing in the characteristic cage-like relation to the cells are demonstrable in the inferior peripheral layer of the tumor. (Fig. 6.) These

Fig 6.



High power view of tumor, showing bands of smooth, fairly coarse, parallel fibrillæ, bent about characteristically at acute angles. Field and staining method same as in Fig. 5.

fibrillæ are in places shown adjacent to the connective tissue which invests the older vessels, and can here be shown to differ in form as well as in staining reaction from the connective-tissue fibrillæ. The fibrillæ are demonstrable in fewer and fewer numbers as one advances toward the core of the tumor; but, whether they are not yet developed or for some reason do not stain, it is not possible to say. The fibrillæ of the peripheral zone can be demonstrated by phosphotungstic acid hæmatein alone (without the preliminary mordanting process) and also by Weigert's method for neuroglia fibrillæ.

The cells are rather large and of an oval or irregularly polygonal shape. The cells of the non-fibrillary core of the mass never show

processes and rarely reentrant angles; but the cells about which the fibrillæ are disposed are often supplied with numerous processes to which fibrillæ may sometimes be seen in close apposition. But few mitoses are demonstrable. There are, however, numerous cells with several nuclei, as a rule centrally set. No ependymal dots have been as yet discovered in the tumor.

(The microscopic examination was carried out in the pathological laboratory of the Boston City Hospital during the service of Dr. F. B. Mallory, to whom we are indebted for supervision of the work.)

Remarks. The report may be summed up as follows:

A new-growth at the base of the cranium gives rise to somewhat characteristic symptoms ending in death after six years. The tumor has gradually filled the interpeduncular space, giving rise in the lower optic apparatus to certain degenerations, a part of which are complete, a part still in process. The brain at large shows little reaction save a subpial gliosis, perhaps incidental to the heightened intracranial tension.

The nature of the growth is in question. The oldest portion of the tumor (judging by the development of the fibrillæ) is in the locus of the posterior lobe of the pituitary gland, which lobe normally contains neuroglia cells developing fibrillæ. The rest of the tumor contains few demonstrable fibrillæ, and could scarcely be differentiated from a sarcoma. It is probably justifiable to classify the case as one of glioma developing in the posterior lobe of the pituitary body. We are not acquainted with previously reported cases of such tumors. Definite proof of the existence of this tumor type can only be brought when some fortunate case shall be dissected showing such a growth in the midst of, or patently growing from, an otherwise normal pituitary body.

A CASE OF DIABETIC GLYCOSURIA WITH INTERCURRENT ICTERUS AND NON-MEDICAMENTAL HÆMATOPORPHYRINURIA.[1]

By Heinrich Stern, M.D.,
of New York.

Dr. R. L., aged sixty-eight years, a retired clergyman, was seen by me in consultation with Dr. Savage on April 2, 1904. The present physician was first consulted in January of this year on the occasion of a slight accident for which local treatment afforded relief. Some weeks afterward a condition bordering on coma

[1] Read at the Meeting of the American Urological Association, Atlantic City, June 8, 1904.

set in. According to the description furnished by the attending physician and the members of his household, the attack was more in the nature of a stupor; Cheyne-Stokes respiration had not been noticed, and the patient defecated and urinated voluntarily. When out of the stupor, however, he could not remember anything at all about it. The condition was looked upon as diabetic in character, as he had been affected with more or less pronounced symptoms of diabetes for the past three or four years. Examinations of the urine made by patient's physician between January and April occasionally showed the occurrence of small amounts of glucose. Other abnormal urinary constituents besides albumin, which was never found, were not looked for. Microscopic examination was not deemed necessary.

In the beginning of March the patient developed icterus. The condition was very pronounced and was accompanied by several attacks, or periods, of chills. Temperature elevation had not occurred, but a subnormal temperature was noted on different occasions. The stools during the icteric period were clay-colored, the urine exhibited the features of the icteric state. The medication was symptomatic, no hypnotics of any kind were prescribed. (Sulphonal, trional, and tetronal were never administered.) Examination by me on April 2d revealed a dilated heart, slight pericardial friction, no valvular disease, normal rhythm, very weak impulse. The lunge were apparently normal. Stomach was slightly dilated, no hardness or structural alteration perceivable. The spleen was normal as to size. Colon and other parts of the intestines were slightly inflated, but fecal accumulations were not present. The liver extended about 3 cm. below the costal arch, the gall-bladder was enlarged and freely palpable. The parts adjacent to the liver were hard and caused pain on deep palpation; nodules could not be distinguished. Adhesions of metastatic processes were not detected. Kidneys could not be palpated. The various reflexes, though diminished, were present. The icterus could not be accounted for specifically; a provisional diagnosis of hepatic cirrhosis was entertained.

The patient complained of excessive weakness in spite of tonic medication. He had been on a light diet, including some cereals, which caused occasional intestinal disorders. The icteric condition was very pronounced and uniform. Examination of the urine exhibited the following facts:

Amount for twenty-four hours 850 c.c.; color very deep red; transparency slightly impaired; odor normal; reaction acid, 0.22°; specific gravity, 1023.5; salts of hydrochloric, sulphuric, and phosphoric acids about normal; salts of oxalic acid somewhat increased; carbamide, 17.85 grams; uric acid, traces; xanthine bodies, traces; creatin somewhat increased; hippuric acid, traces; urobilin, very large amounts; uroxanthin, traces; serum albumin, traces; biliary

acids and fatty matters absent; glucose, glycuronic acid compounds, alcaptonic acids, acetone, and diacetic acid absent. The microscopic examination did not reveal any excessive amounts of normal or any abnormal histologic elements.

The very outspoken dark-red color of the urine and the very large amount of biliary pigment led me to suspect the presence of some other specific coloring substance. Accordingly, the presence of hæmatoporphyrin was looked for. The urobilin, extracted from the urine by a modification of Garrod and Hopkins' process, was treated by the method devised by Saillet. A portion of the acid-ethereal extract was shaken with water. The water takes up the urobilin, but not the hæmatoporphyrin. Another portion of the acid-ethereal pigmentary extract was agitated with 5 per cent. hydrochloric acid. The latter takes up both coloring substances. After separation ammonia was added to the dilute acid; this was reacidulated with acetic acid and shaken with sulphuric ether. By this process the hæmatoporphyrin is extracted, while the urobilin remains behind. The hæmatoporphyrin obtained by the two methods was identified by spectroscopical examination. The examination on the days following after April 2d were made by the first method above described, by dissolving out the urobilin with water.

The presence of hæmatoporphyrin was found for fifteen days longer; daily examinations of the urine were made until March 20th. The amount of hæmatoporphyrin, though, gradually decreased until on the sixteenth day its presence could not be demonstrated any longer. The urobilin, however, continued to be excreted in very large amounts. In none of the specimens of urine examined until April 20th could glucose be demonstrated.

On May 14th I made a second examination of the patient. The icteric condition had greatly subsided, but was still of quite a pronounced degree, the patient, whose diet since April 2d had consisted mainly of milk and milk preparations, had experienced less trouble with his intestines, but felt very weak, and was extremely emaciated, his present weight being 132.5 pounds; two years ago he had weighed 210 pounds. I must mention that the patient's height is over six feet. The urine on this day exhibited no hæmatoporphyrin, but the amount of urobilin was still very large. Glucose was found for the first time on that day, and this to the amount of 7.5 per cent., which, the twenty-four hours' output of urine being 1400 c.c., amounted to 105 grams per day. The patient was put on a very rigid antidiabetic regimen, with the result that on May 21st his urine was entirely free from sugar and he felt himself much stronger. The ferric chloride reaction did not ensue on either occasion. Acetone could also not be demonstrated.

This case is of interest from two points: first, on account of the non-medicamental production of hæmatoporphyrin; and, second,

on account of the synchronous, respectively intercurrent supervention of the three symptomatic manifestations: icterus, hæmatoporphyrinuria and diabetic glycosuria.

Hæmatoporphyrin occurs in small amounts in normal urine and contributes toward its normal color. Its presence in large amounts is always a more or less abnormal phenomenon. Most cases of abnormal hæmatoporphyrinuria have occurred after the administration of sulphonal, trional, and tetronal. Excessive hæmatoporphyrin output is almost a constant symptom in chronic lead intoxication. Abnormal hæmatoporphyrinuria has been found in a case of Graves' disease, one case of hereditary syphilis, one of gastric ulcer with hæmatemesis, and in a few other diseases. In all these diseases its occurrence was accidental, it having been in no relationship with the original disease. According to Nencki and Sieber[1] hæmatoporphyrin and bilirubin are probably of synchronous production—their seat of formation being the liver cells especially. The readily convertible hæmatoporphyrin is utilized for the synthesis of the hæmoglobin molecule; the non-utilizable bilirubin is excreted with the intestinal contents. These deductions stamp the hæmatoporphyrin as a normal intermediary product of metabolism. Other investigators, however, have concluded that inasmuch as the normal bile does not exhibit hæmatoporphyrin, this does not seem to play an important role in the organism, and that it must not be considered an intermediary product of the anabolism or an essential catabolic product in the physiological disintegration of the coloring matter of the blood.

To determine the place of the abnormal production of hæmatoporphyrin, the individual organs of animals poisoned with sulphonal were examined for the presence of hæmatoporphyrin. This was never found in the spleen, blood, muscles, or marrow, but it could always be demonstrated in considerable amounts in the liver. However, as the liver is an important excretory organ of hæmatoporphyrin, its occurrence therein is by no means proof of its hepatogenous formation.

That hæmatoporphyrin was not the result of any of the remedies, there can be no doubt. Plumbism could also be positively excluded. We may assume, therefore, that if the hæmatoporphyrin was of toxic origin, the toxiferous substance was of intrabiontic origin. Whether the same toxic substance stands at the foundation of the accompanying or alternating symptoms, icterus and glycosuria, is a mooted question. I am inclined to accept the interrelation of the three symptoms in this instance. This is confirmed by the fact that while abnormal hæmatoporphyrinuria was present, the glycosuria, which had existed to a greater or lesser degree for some years previously, had ceased entirely, and that after disappearance

[1] Arch. f. experim. Path. u. Pharm., 1888, 24.

of the abnormal amounts of hæmatoporphyrin (how soon after could not be determined as no urinary examination was made between April 20th and May 14th), the glycosuria reappeared, occurring probably in greater intensity than ever before. It appears almost as if one and the same anomaly was the causative factor of the three manifestations, that while icterus set in when chronic glycosuria was present, this disappeared when hæmatoporphyrinuria supervened, and did not recur until the hæmatoporphyrinuria had again vanished. It seems that the disappearance of the glycosuria was dependent upon the presence of the hæmatoporphyrinuria; that is, that the anomalous condition underlying both symptoms could only bring about either of them at one time.

The case stands isolated, as I have not found in medical literature any allusion to the synchronous or respectively the intercurrent occurrence of these three phenomena. Operative interference may be required to relieve the tension of fluid in the gall-bladder. A more detailed study of the case will follow at a later day.

AN UNUSUAL OVARIAN CONDITION.

By Lewis Schooler, M.D.,
of Des Moines, Iowa.

The patient, whose case is here reported, was the wife of a miner and has been brought up amid the surroundings of the ordinary coal-miners' camp, with nothing of importance in either the family or personal history. She was the patient of Dr. Charles F. Smith, and I saw her in consultation with him about three weeks previous to time of the first operation. At that time she believed herself pregnant and sought an examination for the purpose of ascertaining whether she would be able to carry the child to term.

After a careful and painstaking examination I advised her to the effect that her pregnancy would not be interfered with by what I then believed to be a diseased Fallopian tube, but which I now know was an extensively drawn-out left uterine cornua. My opinion was most unsound, as she miscarried about ten days later and at a little more than the third month. This accident was not followed by any bad results, and she recovered very nicely after the miscarriage.

Urinary examination showed that fluid to be acid in reaction, specific gravity 1016, color light amber, cloudy, total solids 37.28 grams per 1000 c.c., albumin and sugar absent.

Mrs. W., aged twenty-four years, married, mother of two children, previous health good, entered the Methodist Hospital August 21, 1903. Condition at time of admission was as follows: Tem-

perature 98.4°, pulse 59, respiration 18; on the day following the temperature at 10 A.M. was 99.6°, pulse 80, respiration 24, and at 4 P.M. temperature 99.4°, pulse 66, respiration 19. Bowels moved freely after the administration of one ounce of castor oil.

From this date until August 27th there was not much change in the patient's condition except that pain, increased pulse rate with slight elevation of temperature, became gradually more marked, and the tumor in left side enlarged perceptibly; the bowels acted fairly well, but were assisted by castor oil every other day, and as there seemed to be no hope of improvement under medicinal treatment, operation was had on the 27th. The incision was begun in the median line a little higher than the point usually selected for an ordinary ovariotomy.

When the fingers were introduced it was discovered that the uterus was dragged upward and to the left, and the Fallopian tube felt like a firm round cord double its normal size, extending from the uterus to the enlarged and displaced spleen, which was firmly attached and admitted of no displacement. The incision was extended upward and the spleen brought into view. It was at least six times its normal size, black and glistening like an old blood clot, but firmer.

The hand was swept entirely around its base, which left no doubt as to the identity of the organ, but in order to further demonstrate the certainty of the diagnosis the capsule was opened and a small piece removed for microscopic examination, which resulted in confirmation of what has been stated above. At the lower pole there was complete and firm union of the spleen, ovary, and fimbriated extremity of the tube. So close was this union that it required close inspection to identify the different structures. The tube, ligament of the ovary, and the upper edge of the broad ligament, were hard and firm on account of the tension. It was then decided to divide them between two ligatures and close the abdomen, and while this was being done it was found that the spleen was bleeding rather freely from incised point and required packing with gauze. Healing by first intention occurred throughout, except where the gauze protruded.

The patient left the table in good condition at 3 P.M., the operation having lasted but thirty minutes, but at 5 P.M. the pulse was 112, and at 12.30 A.M. it was 140, and went up to 146 at 2 A.M., which was the extreme reached at any time. The temperature was 101°. Morphine, required on account of pain, and normal saline solution in large quantities were given at this hour. The pulse improved, and at 8 A.M. was 120; temperature 100°.

From this time there was nothing of interest in the case and she left the hospital September 11th.

Four weeks later she was seen at her home and was suffering from obstruction of the bowels, which disappeared on the following

day. At this time the spleen was apparently reduced in size at least one-half. She was admitted to the Mercy Hospital November 17th with complete obstruction of the large intestine, and was operated on at once, the incision being in the left semilunaris.

The obstruction was due to extensive adhesions almost the entire length of the descending colon. They were ligated at several points and the bowel freed and filled with normal saline solution through the rectum. The uterus was normal in size and position. The spleen was in like condition and, instead of the intensely black color present at the time of the first operation, was normal in appearance. The patient made a good recovery and left the hospital on November 30th in apparently good condition, with the bowels acting normally and free from pain. To me this experience is unique.

How two organs normally so far apart and with a limited amount of mobility got together and stayed together, I cannot explain. If it was a wandering spleen, what caused it to return to its normal site, and up to the present time to remain there? The patient had never suffered from malaria and the blood count showed no anomaly in that direction.

Previous to the second operation, I was perfectly contented with the explanation of a floating spleen, but the revelation of the last operation has caused me to give up that theory.

STUDIES UPON THE CAPSULE OF THE KIDNEY.

By Haven Emerson, A.M., M.D.,
of New York,
Fellow of the Rockefeller Institute for Medical Research in the Departments of Physiology and Pathology in the College of Physicians and Surgeons of Columbia University, N. Y.

From the physiological standpoint, the fibrous envelopes or capsules of organs have received but scant attention, and it was a desire to make some addition to the facts known about such capsules that led me to make the following studies.

Among the organs studied the results obtainable have been most definite in the case of the kidney, partly because of the distinct existence of the kidney capsule, and partly because of the greater convenience of manipulation, due to the size and location of the organ, than is the case with other organs, such, for instance, as the pancreas or the submaxillary gland.

Observations upon the capsule of the kidney have become especially interesting, in view of the present discussion of surgical procedures which depend for their effect upon an alteration of the normal relations of the capsule and its blood supply to the functions

and structure of the kidney parenchyma. The following studies were made upon dogs, rabbits, and a pig:

The capsule of the kidney is made of firm connective tissue with a moderate amount of yellow elastic fibres. It is arranged in two layers, the outer thick and dense, the inner represented often by only a single layer of cells. The inner layer is always adherent, even when the capsule is roughly removed, and is continuous with the intertubular connective tissue. Vascular connection with the peritoneum covering the capsule is slight, the main blood supply to the capsule being from the kidney parenchyma by abundant bloodvessels of considerable size, distributed irregularly over the surface of the kidney. The capsule seems to serve as a support, and as a protection against injury and pressure from without.

My first experiments were devised to ascertain whether the capsule would allow or prevent the absorption into the blood of salts in solution. My second series aimed at determining the result of decapsulation of the kidney, upon the animal and the organ.

Part I.

Medium and small dogs were used, 5 to 9 kilos in weight. Males were preferred because the internal generative organs of the female make the catheterizing of the ureters difficult. The animals were kept on a fluid diet of soups and milk for forty-eight hours before the operation.

Various containers for the kidney were tried, in which the kidney might rest immersed in a liquid and yet suffer no constriction of its vessels and ureter at the hilus, while at the same time allowing no escape of liquid into the peritoneal cavity at large. The only satisfactory object was found to be an oblong bag of rubber tissue.

Ether narcosis was used, often preceded by a small subcutaneous dose of morphine sulphate (0.4 to 1.0 dg.). Tracheotomy was performed in all cases for convenient anæsthetization. With the animal in the dorsal position a median abdominal incision was made from the ensiform cartilage to the penis, with a lateral incision at right angles to the former cut, just below the free border of the ribs on the left side, the left kidney being more conveniently located for experiment than the right. The kidney was then exposed. Its peritoneal coat and fat were stripped off to the hilus, and then, with or without decapsulation, the organ was enclosed in the rubber bag. The removal of the capsule was done by elevating a portion with a sharp hook, cutting under the hook and separating the capsule from the parenchyma with a blunt, flat, smooth seeker. The open end of the rubber bag was passed over the kidney and clamped about the hilus, leaving vessels and ureter ample room. The bag was then drawn back until it fitted the kidney snugly, leaving the hilus free, about three-fifths of the sur-

face and bulk of the kidney remaining within the bag. The blind end of the bag was fitted with a glass tube, over which a short piece of rubber tubing provided with a clamp was slipped. The bag was then filled with 50 c.c. of warm normal saline solution, and the kidney was allowed to assume its normal position. One or both ureters were catheterized by glass tubes, bent so as to empty into test-tubes near the dog's side.

If it was found, then, that all bleeding from the surface of the kidney had ceased, that there had been no leaking from the bag, and that the kidney was secreting, the saline solution was drawn off, the bag was filled with the test solution, and the urine was collected at short intervals and tested. The phenomena observed on stripping the capsule from the kidney are described in Part II.

Of the twenty-four animals used for these experiments the results had to be thrown out in two cases because of leaking of the test solution from the bag into the peritoneal cavity. Control tests were always made of the peritoneal fluid to prevent error from possibility of absorption through the peritoneum instead of the kidney. In four cases I failed because the bag was too tightly applied, and constriction of the parenchyma caused compression of urine; in two cases because the intestines were too much distended to allow of delicate manipulation; in one case because of uncontrollable bleeding from an abnormally located renal vein. The remaining fifteen gave the following results:

Potassium iodide was used with three animals upon kidneys possessing normal intact capsules, in solutions of 1 per cent. and 10 per cent. for one-half to two hours, and in no instance was iodine found in the urine (the test for iodine being made with fuming nitric acid and chloroform). In two animals the same strength of solutions were used upon kidneys possessing newly formed capsules thirty-nine and forty-four days after decapsulation, with the same negative results.

For the sake of brevity the term normal kidney will be used to signify a kidney possessing an intact capsule as distinct from a decapsulated kidney. No diseased kidneys were found.

Similar solutions were used upon the freshly decapsulated kidneys of two animals, and iodine was found in the urine in twenty minutes. In two animals potassium iodide in 10 per cent. solution to the amount of 100 c.c. was injected into the femoral veins, while the bag enclosing the freshly decapsulated kidney contained normal saline solution. The saline solution was tested at intervals for one and one-quarter hours, and, although there was an abundance of iodine in the urine, none appeared in the solution in the bag.

Sodium salicylate in 10 per cent. solution was applied by means of the bag to the normal kidney for one and one-half hours with negative results. A similar solution applied to the freshly decapsulated kidney resulted in the appearance of the salt in abundance

in the urine in twenty-five minutes. In a 1 per cent. solution, applied for one and three-quarter hours, to the decapsulated kidney, the sodium salicylate did not appear in the urine. In the last two cases the secretion of urine became distinctly diminished on application of the solution of sodium salicylate, and this diminution reached such a degree in the last case that not enough urine was secreted to afford a test after the first half-hour, there being a cessation of secretion without any congestion to account for it.

Potassium ferrocyanide in 10 per cent. solution was applied to the normal kidney with negative results. Applied to the freshly decapsulated kidney, its presence was detected in the urine in forty-five minutes.

Potassium cyanide in 0.6 per cent. solution was applied to the normal kidney with no effect upon the general condition of the animal. When a 3 per cent. solution was applied to the normal kidney, irregular and frequent heart beat and shallow, feeble respiration were noted in a half-hour. The 0.6 per cent. solution was used upon a freshly decapsulated kidney, and in ten minutes there was a marked irregularity of the heart action and respiration. The solution was then removed and the animal recovered.

Methylene blue in saturated solution and in solution of 1 per cent. and $\frac{1}{60}$ per cent., when applied to the normal kidney, gave no evidence of its absorption during two hours. When tried upon the freshly decapsulated kidney for the same length of time the same solutions also gave negative results. When 60 c.c. of a $\frac{1}{60}$ per cent. solution were injected into the femoral veins no blue color appeared in the clear saline solution in the bag surrounding the decapsulated kidney, although the urine secreted during the time of observation was deeply stained. Immediately after the exposure of a freshly decapsulated kidney to a saturated solution of methylene blue for two hours the kidney was removed and frozen sections were cut and examined at once. A thick, superficial lymph clot, which forms on the surface of the kidney after decapsulation, was found to be stained blue, and there was a delicate staining of the connective tissue of the parenchyma as far as the more superficial glomeruli.

SUMMARY OF PART I.

It is apparent that when the kidney capsule is intact absorption does not take place in sufficient amount to be appreciated by chemical tests in the urine, and that only when a strong solution of a powerful systemic poison was used was there any indication of the test substance in the blood stream, as shown by constitutional symptoms.

It is also evident that, when the capsule was stripped, of the five substances tested three appeared promptly in the urine; one, potassium cyanide, showed a marked constitutional effect, and one, methylene blue, failed to be appreciated in any way. It seems

likely that if the circulatory disturbance had not caused a marked cessation of urinary flow potassium cyanide would also have been absorbed into the renal tubules. With methylene blue the lymph clot formed upon the denuded kidney surface appeared much more quickly than with the other solutions employed. The surface through which absorption might occur was thus rendered much less accessible to the solution, and to this condition we must ascribe the negative result. The fact that there was a discoloration of the parenchyma as far as the glomeruli gives warrant for believing that absorption was under way, though in a slight degree. From the appearance of the surface of the kidney two to three hours after decapsulation, it would be hard to believe that more absorption would occur after that time than would take place with the capsule intact. It may be worth noting here that the results of my experiments suggest that the use of strong antiseptic solutions in the vicinity of a decapsulated kidney may do harm by direct absorption into the kidney parenchyma. They thus furnish a reason in addition to those accepted for surgical technique for limiting the fluids, allowed to come in contact with such an organ, to sterile water or physiological salt solution.

Part II.

While watching the experiments, already described, it was apparent that an attempt at repair of the injury inflicted by decapsulation was already begun in the half-hour to three hours while the dogs were under observation. The fifteen dogs which suffered decapsulation for the sake of immediate observation of absorption showed the various stages, from multiple hemorrhages, due to the rupture of the capsular bloodvessels, to the formation of a firm, smooth, elastic lymph clot, destined to assist in the formation of a new fibrous envelope. Except in rare instances, where there is unusual vascular distribution, the hemorrhage resulting from removal of the healthy capsule in the dog ceases in about five minutes. Exudation of lymph from countless points over the whole surface of the kidney follows decapsulation, and in a half-hour there is formed a smooth, clear, jelly-like coat. This film at first thickens unevenly, and then gradually becomes cloudy as the fibrin network is established, until at the end of two hours there is a firm, tenacious, slightly adherent lymph clot protecting the denuded surface. For the later effect of decapsulation we may turn to the following operations and autopsies:

Eight dogs, six rabbits, and one sow were used. Of the dogs I failed in one because of asymmetry of one of the renal veins, which entered high upon the side of the kidney instead of at the hilus; and in one from an error in following the muscular guide in my incision, and resulting hemorrhage. The remaining six showed no sepsis,

the wounds healing cleanly and promptly. There was at no time any abnormal condition of urine of any of the animals. They were autopsied at various intervals from thirty-nine to three hundred and thirty-nine days after operation, and without exception were in perfect condition when killed. (For the number of days after decapsulation in each case, see report of autopsy.) In the cases of the dogs the operation was by the lumbar incision. The kidney was drawn into the wound by its perirenal fat, and held there by pressure from below until the capsule was stripped, in the manner already described. It is a matter of some difficulty to decapsulate the kidney of a dog without entering the peritoneum, but in Cases IV. and V. especial care was taken, and in Case V. the whole operation was done extraperitoneally. This difficulty is due to the almost complete investment of the kidney with peritoneum, the perirenal fat being usually very scant.

Of the six rabbits, one died in four days from occlusion of the ureter, which resulted from an attempt to bind the decapsulated kidney to a lobe of the liver by silk sutures. Three of the remaining five were operated upon by the lumbar method, and the capsule stripped without entering the peritoneal cavity—a procedure not at all difficult in the rabbit. In the other two I opened the abdomen in the midventral line and decapsulated the kidney without precautions except as to injury of other viscera. Each of these rabbits developed a ventral hernia, due to the use of plain catgut in sewing the muscular layer of the abdominal wall. None of them suffered any sepsis or appeared otherwise than healthy, except for the presence of what appeared to be an eczema of the nose and skin of the face during the month before autopsy.

The operation upon the sow was done by a lateral abdominal incision, and the capsule was stripped intraperitoneally. The animal increased from one hundred and fifty to three hundred and fifty pounds between the time of operation and the date of autopsy.

At the time of autopsy several of the kidneys were injected with blue gelatin mass in the following manner: The kidney, with whatever structures or organs were adherent, was placed in a bath of 0.85 per cent. salt solution at a temperature of 99°. Cannulas were inserted into the artery and one vein at the hilus, the other vein or veins being then clamped. The kidney was then washed free from blood by forcing saline solution through first the artery and then the vein at a pressure of 180 mm. to 200 mm. of mercury and at the temperature of 99° to 100°. Then a thin gelatin mass stained deeply with Berlin blue was forced through under the same conditions of pressure and temperature for an hour or more by the artery and then for an equal time by the vein. The artery and vein were tied and the kidney was packed in ice until the gelatin had hardened.

All specimens were hardened in equal parts of Müller's solution

and 5 per cent. formalin, and the stains used were either hæmatoxylin and eosin or the carbol fuchsin.

The gross and microscopic findings upon the six dogs, five rabbits, and the sow follow:

Case I.—Mongrel, adult male, 10.5 kilos, thirty-nine days after decapsulation of the right kidney intraperitoneally by the lumbar method. The left kidney presented nothing abnormal. Adhesions were found on the right side between the right kidney and the left lobe of the liver about one-half inch long, also to the omentum, the latter not only over the decapsulated area, but at the hilus as well, where only the peritoneum had been stripped. Slight bleeding occurred on separating the adhesions, and this, apparently, wholly from the liver and none from the kidney. The animal was kept under ether an hour to study the circulation. The newly formed covering of the kidney was found more adherent than normal, though quite soft and tearing the parenchyma slightly when stripped.

Microscopic. The normal kidney shows an even capsule, an inner thin cellular layer, and an outer thicker fibrous connective-tissue layer. The decapsulated kidney shows a newly formed connective-tissue envelope, in some places thinner, elsewhere from three to five times thicker than normal. The outer layer has abundant round cells loosely embedded in young connective tissue. The inner layer still marked, evidently not stripped off at the operation, but its character much less distinct at the site of the adhesions, where it appears to have been absorbed, and where occasional wedges of round cells are seen crowding among the urinary tubules. The whole newly formed coat appears but slightly vascular. No changes appear in the renal parenchyma.

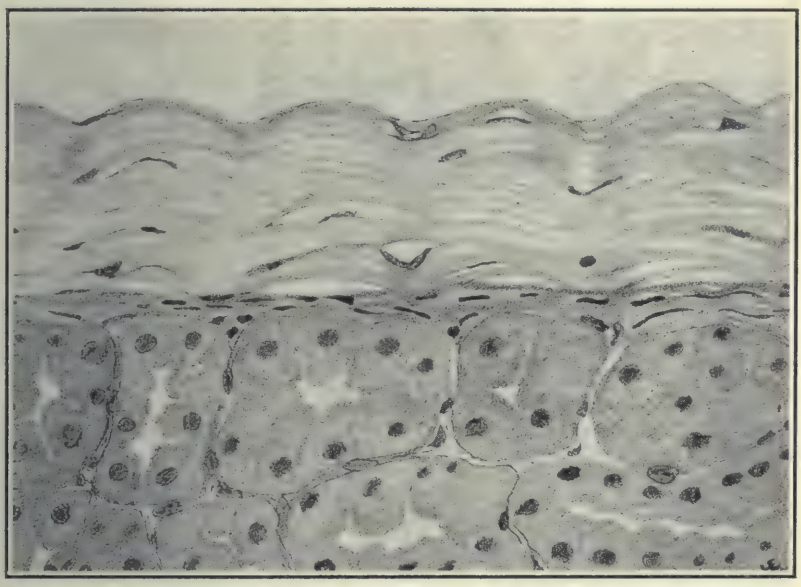
Case II.—Adult male fox-terrier, 8 kilos, autopsied one hundred and forty-four days after decapsulation of the right kidney intraperitoneally. Left kidney showed nothing abnormal. (See Fig. 1.) Firm adhesions were found between the right kidney and the left lobe of the liver, the pancreas, the mesentery, and the large intestine. Marked absence of bleeding was noticed on tearing the attachments except where the pancreas is adherent. This attachment is so close that it cannot be separated without tearing off the newly formed capsule. The surface of the kidney is irregular, appearing like the granular kidney seen in chronic interstitial nephritis in man. The capsule cannot be removed without tearing the parenchyma.

Microscopic examination shows essentially the same variation from normal as in Case I., with the following differences: The inner capsular layer is strikingly absent where adhesions are formed and especially at the site of the pancreatic attachment. Elsewhere the inner layer is thicker than normal. The outer layer and capsule as a whole are everywhere much thicker. (See Fig. 2.) Small, newly formed vessels, such as are found in granulation tissue, are

seen in loosely arranged connective-tissue bundles between the pancreas and the kidney. Tubules which reach the surface of the kidney are in places distorted and crowded by the encroachment of connective-tissue cells, this invasion of the parenchyma in some places taking form of distinct wedges. In some places are found cup-shaped depressions, with destruction of considerable areas of tubules and glomeruli, the whole degenerated tract appearing strangled by the network of contracting connective tissue.

Case III.—Small male, mongrel puppy, 5 kilos. Examined two hundred days after decapsulation of the right kidney intraperitoneally. The left kidney appears normal. Adhesions to the pan-

Fig. 1.



Normal (left) kidney of Case II.

creas, the liver, and the posterior abdominal wall almost completely cover the kidney surface. The viscera are connected not by bands, but directly surface to surface. The muscular attachment is by a dense, non-vascular band impossible of separation without tearing off the newly made capsule and some of the renal parenchyma. This kidney was injected with gelatin mass, as described above. From the cut surfaces of the pancreas and liver the blue mass flowed freely during the whole period of injection.

Microscopic examination shows the following: A section of the kidney at a point where no adhesions were formed shows a much thickened capsule of new dense connective tissue, with small blood-

vessels injected with the blue gelatin mass directly connecting with the capillaries of the renal parenchyma. Deep wedges of round

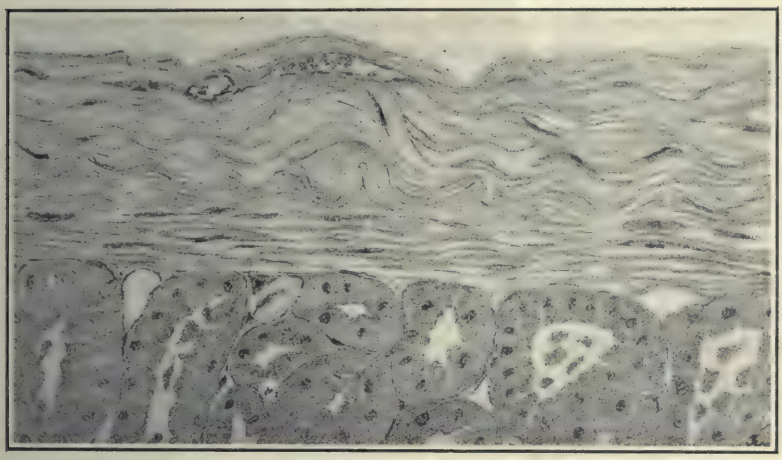
FIG. 2.

Decapsulated (right) kidney of Case II., showing thickened capsule.

connective-tissue cells enter from the capsule as far as the nearer glomeruli.

A section at a point where the liver is in intimate contact with the kidney shows in some places a thin layer of dense connective tissue of the thickness of the inner layer of the normal capsule, and no vessels communicating between the two viscera. In other places is seen a marked injection of liver capillaries and also injected vessels in the connective tissue between the two viscera. At some points there are but two extremely thin layers of flat connective-tissue cells separating the viscera from each other. At frequent points along the renal cortex are seen deep connective-tissue wedges distorting, destroying, and occluding the tubules, and in some instances even completely surrounding the glomeruli. Degeneration of the tubular epithelium is present in all such areas. (See Fig. 3.)

Fig. 3.



Decapsulated (right) kidney of Case III., showing cup-shaped depression with tubular and glomerular degeneration and replacement fibrosis.

Where the pancreas is adherent to the kidney the connective tissue separating them is thicker than where the liver is adherent; otherwise the conditions are the same. Blue injection mass is seen in the smaller vessels and capillaries at various points in the pancreas.

Case IV.—Brown and black mongrel, 7.5 kilos. Autopsied two hundred and forty-five days after extraperitoneal decapsulation of the right kidney. To ensure the kidney remaining in position three plain catgut sutures were used at the time of operation to bind it to the muscular wall at the site of the wound.

Through the courtesy of Dr. Isaac Levene I had an opportunity to observe oncometric records of this kidney with and without the use of adrenalin intravenously. The character of the tracings was

identical with that of the tracings from a normal kidney under the same conditions.

The only attachments were to the perirenal fat and the muscular wall of the abdomen.

The left kidney showed no alterations of the capsule or of the parenchyma, the inner layer of the capsule being about one-half to two-thirds the diameter of a convoluted tubule in thickness, and the whole capsule two and a half to three and a half the same diameter. No interstitial infiltration or epithelial degeneration.

The right kidney has a capsule freely supplied with large and small vessels, some with well-defined walls. The blue gelatin mass shows free connection between the intertubular capillaries and the blood spaces and vessels in the loose reticulum of the new capsule. The new capsule varies from normal thickness with a very dense structure to a loose network as much as fifteen times as thick.

Unevennesses of the capsule correspond to marked irregularities in the kidney surface, the usual even arrangement of tubules being broken by depressions, where connective-tissue processes invade the parenchyma.

There is a uniform degeneration of the outer layer of tubules, accompanied in some places by absorption. A few glomeruli are found surrounded by new connective tissue. The deeper layers of the kidney appear natural. Upon the surface of the kidney are found abundant tufts of young connective tissue with a free blood supply running into the perirenal fat. Where the capsule is relatively thin and dense the blood supply is scanty, quite as few blood spaces being found as in a normal capsule.

At the site of the adhesion to muscle there is a mass of connective tissue of a firm type with a free vascular supply. In this area, 5 x 7 mm., the tubules are distorted, compressed, and drawn up, as it appears, out of the adjacent kidney tissue by the contracting connective tissue. Compression, flattening, and degeneration of tubules and glomeruli are seen in bulk. This is probably the location of one or more of the retention sutures. Adjacent to this area is a part of the capsule which shows no variation from normal in thickness or vascular supply and could not be distinguished from normal except by a lack of definiteness between the inner and outer layers.

Case V.—Black mongrel, 7 kilos. Autopsied two hundred and fifty-one days after decapsulation of the left kidney. Care was taken to do this decapsulation extraperitoneally, but without success. The dog was pregnant at the time of the autopsy.

The left kidney was adherent to the muscle of the wound and to the mesentery.

The right kidney appeared normal, and on section showed no variations from normal in capsule or parenchyma.

The left kidney shows an uneven capsule varying from one-half

to four times normal thickness, except at the site of the attachment to the muscle of the lumbar wound. Vascularization of the capsule generally is slight, the tissue being dense and with but few round cells. The adhesion between the kidney and the muscle is 2 mm. long, highly vascular, with a few masses of dense connective tissue. At this point connective-tissue invasion of the parenchyma is noticeably greater than elsewhere in this kidney.

Case VI.—Small brown terrier, 6.5 kilos. Autopsied three hundred and thirty-nine days after decapsulation of the left kidney intraperitoneally. This dog had had a litter of pups, and was again pregnant at the time of autopsy.

The right kidney shows no variations from normal in the capsule or the parenchyma.

A few adhesions to adjacent fatty tissue were found, but none to any viscera from the left kidney.

The left kidney shows a firm, fairly even capsule for the most part, but slightly thicker than normal. At places, however, the capsule is as much as five times the normal thickness. Blood-vessels are very rare in the firm, thin parts of the capsule, and are present in fair size and number only where the capsule is thick and loosely constructed. Young round cells are present only in the thicker parts. In other words, over the greater part of the kidney we find a capsule resembling the normal intact capsule in every respect, except in the definiteness of the layering of its tissue. It is, however, to be noted particularly that exactly where the abnormal thickness and vascularization of the capsule persist we find the invasion of the parenchyma by connective tissue with resultant degeneration and atrophy of the tubules.

Everywhere, even under the more normal-appearing capsule, are evidences of pressure and contraction, causing an unevenness of the cortical layer of tubules.

Case VII.—Brown and white buck rabbit, autopsied fifty-nine days after decapsulation of the right kidney.

Case VIII.—Slightly larger brown and white buck rabbit, autopsied eighty-four days after decapsulation of the right kidney. The gross appearances are identical in both, there being no adhesions to other viscera, as the operations were wholly extraperitoneal. The perirenal fat is more firmly bound to the operated than to the normal kidney. A slight milkiness and a perceptible difficulty in stripping the newly formed capsule were all that distinguished the operated from the normal kidneys.

Microscopic examination of Case VII. shows the layers of the normal capsule less marked than in the dog. The newly formed capsule presents the characteristics of young connective tissue. It is thicker than normal by four or five diameters. Round cells are abundant throughout. No vascular connections with the parenchyma are found, and there is no infiltration of the parenchyma with

connective-tissue cells. The new capsule has formed under the intimately attached perirenal fat. Microscopic examination in Case VIII. shows exactly the same state of things, except that the outer layer of the new capsule is denser and the cellular elements are less marked.

Case IX.—Adult brown buck rabbit, autopsied one hundred and forty-eight days after decapsulation of right kidney by the abdominal intraperitoneal method.

The left kidney was normal in its relations, and on microscopic examination showed normal capsule and parenchyma.

The right kidney was adherent to the intestines by loose bands of connective tissue and to the liver, intimately, surface to surface. The newly formed capsule is made of loose, young connective tissue with a few areas of much thinner, denser tissue, especially at the site of the adhesions to the liver. Where the capsule is of loose structure there are a few small capillaries, but elsewhere the capsule appears about as little vascular as in a normal capsule. There are few regions of penetrating connective-tissue wedges, but these are characterized by all the usual appearances, and the tubules at the cortex are very generally the seat of cell degeneration. At a few points over the surface of the liver attachment there is an invasion of connective tissue among the liver cells, with resultant cell degeneration. There was no evidence of vascular connection with the liver, although the capsule at several points, where it is loose and thick, shows frequent injected vessels.

Case X.—Adult brown buck rabbit, autopsied two hundred and forty-one days after decapsulation of the right kidney by the abdominal intraperitoneal method.

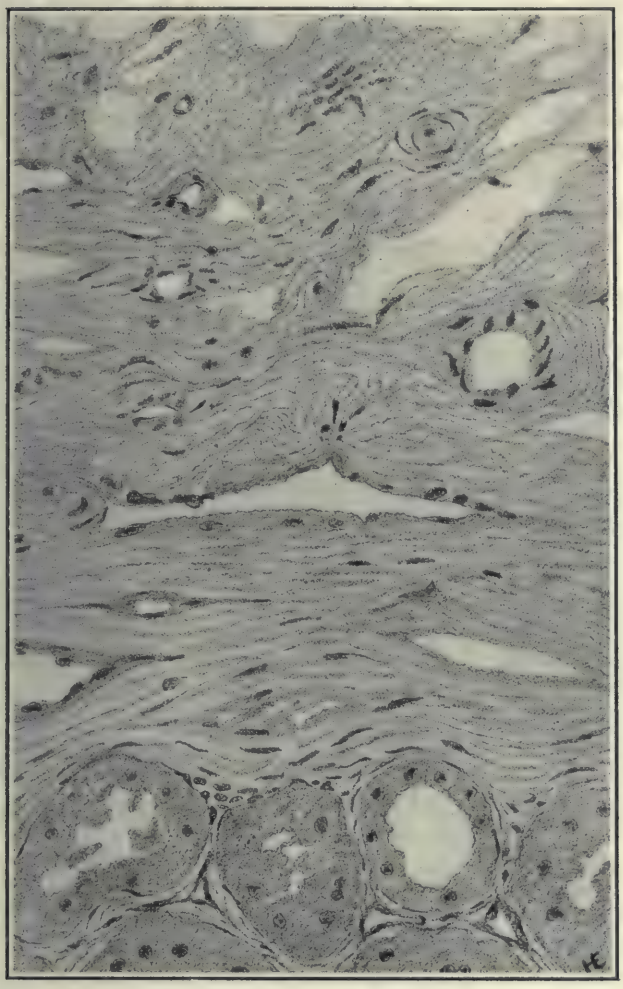
The left kidney is normal in every respect—macroscopically and microscopically.

The right kidney is adherent to the under surface of the liver and very firmly to the fatty capsule. No marked vascular supply. Section through liver adhesion shows slight injection of liver capillaries at several places, with occasional small vessels in the thick capsule. The capsule varies from one-third to six times normal in thickness, and is characterized by dense and non-cellular structure. There is no intertubular interstitial increase, but the tubules are dilated and filled with cell detritus; the epithelium is flattened, and the nuclei stain poorly and lack definiteness. These changes are less marked the farther we go from the cortex. The glomeruli are not affected. Where the absorption of the new capsule between the liver and the kidney had gone so far as to leave but a single layer of spindle-shaped cells, there were several small masses of round cells invading the liver substance.

Case XI.—Gray female rabbit, autopsied two hundred and seventy-five days after decapsulation of the right kidney by abdominal intraperitoneal operation.

The left kidney presents no variations from normal. (See Fig. 4.) The right kidney shows a few light adhesions to the fatty capsule and the mesentery.

FIG. 4.

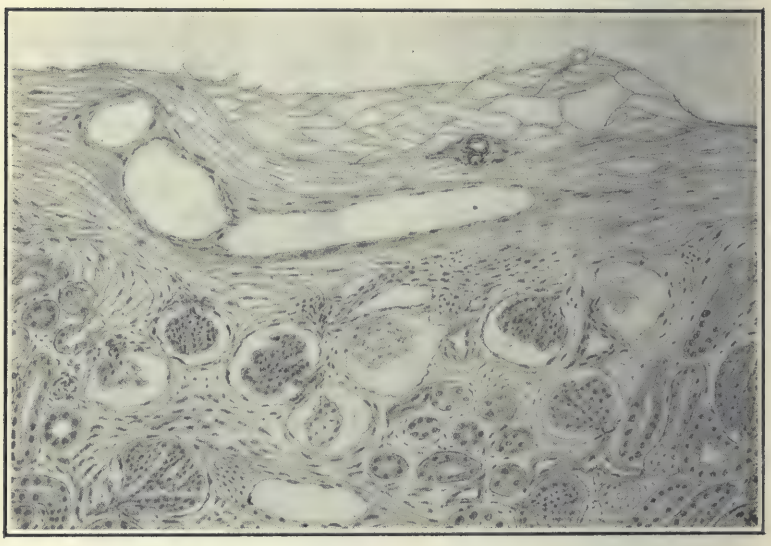


Normal (left) kidney of Case XI.

Everywhere over the surface of the kidney, except at the site of the few adhesions, the capsule varies but slightly from the normal in thickness. Where the capsule is of normal thickness the structure is denser and slightly more cellular, but no more vascular than normal. The adhesions are well supplied with organized blood-

vessels. The parenchyma has suffered severely. In a section exposing one-third of the transverse circumference of the kidney are found seven distinct wedges of new, round-cell connective tissue invading the cortical tubules from the capsule. Three of these wedges extend half-way to the hilus, and are lost in the intertubular tissue among the straight tubules. In the path of these tracts are found all grades of compression and degeneration of tubules and glomeruli, from a cloudiness and constriction of the deeper tubules to a complete replacement fibrosis just beneath the capsule. There is a noticeable increase of bloodvessels in size and number in these connective-tissue wedges. (See Fig. 5.)

FIG. 5.



Decapsulated (right) kidney of Case XI., showing a typical connective-tissue wedge.

CASE XII.—White sow, autopsied two hundred and forty days after decapsulation of the left kidney by the abdominal intraperitoneal method.

The right kidney is normal in every respect. The capsule resembles the rabbit kidney in being loosely attached and thin. Evenness of arrangement of the tubules and a full regular and sharply defined appearance of the tubular epithelium characterizes the parenchyma.

The left kidney has light adhesions to the perirenal fat, to the mesentery, and to the omentum. These are tough and do not bleed when torn. Changes are seen in the capsule similar to those noted in the decapsulated kidneys of other animals. Uneven thickening

varying from two to ten times the normal thickness, and an irregular and occasionally free vascular supply, less where the capsule is densest and where there are no adhesions. Vessels can be made out communicating between the capsule and the adhesions. In the parenchyma there is a widely distributed round-cell infiltration from the capsule, deep among the tubules, with occasional wedges penetrating farther among the glomeruli. Cellular degeneration is not found to a great degree among the tubular epithelium, but there are regions, chiefly at the surface of the kidney, where the effect of pressure is shown by disintegration of cell bodies. Where the interstitial increase is greatest are found more abundant intertubular vessels, but it is with difficulty that even small vessels are to be found penetrating the capsule from the parenchyma of the kidney.

Reports of Previous Experimental Studies.

Without entering the tempting field of medical speculation as to whether decapsulation does or does not benefit the kidney, already the seat of a chronic inflammatory condition, I shall confine my report to the results of experimental investigations undertaken to assist the clinician and the surgeon.

Albarran and Bernard[1] studied the kidneys of rabbits from fifteen to sixty days after decapsulation by the lumbar method. They found a few minor changes of degeneration in the tubules near the surface and the prompt formation of a new capsule denser than the original. They conclude that the effects of relieving congestion by decapsulation of the kidney, claimed by some operators, must be transient when the rapid re-formation of a denser capsule so soon follows the removal of the original one.

Boutch-Osmoloffski[4] also studied rabbits after decapsulation by both the lumbar and abdominal method. He found marked proliferation of new connective tissue into the parenchyma within six days after decapsulation of the kidney. Twelve days after decapsulation he found marked connective-tissue growth, but not deeply into parenchyma. He found that the kidney tissue at the surface undergoes marked atrophy and replacement fibrosis, but found no newly formed vessels.

Johnson[9] found in dogs that decapsulation of the kidney results in the formation of a new fibrous capsule usually thicker than normal, but varying greatly in thickness. He found occasional infiltration of round cells into the renal cortex, but no effect upon the glomeruli. He found no anastomoses between the renal and the perirenal bloodvessels. He concludes that there is no experimental evidence to support the vascular hypothesis for the cures claimed in cases of chronic Bright's disease, treated by decapsulation of the kidney.

On the other hand, Bassan,[3] in his very complete monograph on surgical intervention in medical nephritis, says that decapsulation

appears well adapted as a surgical treatment of Bright's disease, because of the probable creation of new paths of blood supply to the diseased organ. Without giving any facts to support this statement he says that his own, as well as the experiments of Claude and Balthazard,[5] favor this view.

Claude and Balthazard[5] do claim to have found important venous and lymph channels in the organized perirenal adhesions, but they give no definite proof that these vessels actually communicated with the renal parenchyma. They state explicitly, however, that although urinary secretion is maintained well and with less cardiac exertion after decapsulation than before, if improvement is to follow, we must have normal epithelium, or else the relief from circulatory pressure will be of no avail. The cases of Claude and Balthazard were studied twenty-five to thirty days after decapsulation.

Fabris[7] concludes from experimental decapsulation in animals that a new capsule is formed in thirty days. This capsule is firm and tough, and has but a slight additional supply of new blood-vessels. He adds that decapsulation may help a unilateral acute nephritis, but that in bilateral and chronic disease it can but be of little or no value.

Ferrarini[8] concludes from numerous experiments upon healthy animals that decapsulation of the kidney causes no functional disturbance or anatomical lesion. The newly formed capsule results from perirenal inflammation accompanied by vascular connection from the capsule to the stellate and medullary veins of the kidney.

In a series of decapsulations of rabbits' kidneys, after acute degenerative processes had been established by the use of irritant drugs, he concludes that there are no essential differences between the normal and the operated kidneys. The observations were made from six to sixteen days after decapsulation.

Anzilotti[2] observes in dogs and rabbits that a new capsule is formed in fifteen to twenty days after decapsulation. In various cases from twenty-four to one hundred and fifty-eight days after decapsulation he finds the new capsule thickened, the tubules distorted, and their epithelium degenerated, the glomeruli undergoing necrosis, and new vessels in the kidney tissue and the capsule.

In a second series he caused a degree of replacement fibrosis in the kidneys by temporary interference with the renal blood supply, and subsequently decapsulated one kidney. He concludes that decapsulation may cause a notable improvement in such a kidney by improving the circulation and causing a regeneration of kidney tissue.

The observations were none of them over a longer period than the cases noted by him in normal kidneys.

Anzilotti's report of observation of regenerated epithelium seems a little fanciful and is not supported by any illustrations of the

tissues so affected. If this degeneration takes place as Thorel[11] also thinks, even in two to eight days after the use of chromic acid or bichromate of potassium as an acute poison, he sees it occur without decapsulation—a fact which, if correctly observed, would scarcely argue for decapsulation.

In regard to the freedom of circulation through the kidney immediately after decapsulation, reference to the oncometric results reported by Dr. Levene[10] show that this is very marked for one or two days after decapsulation, but a similar test made on Case IV., reported above, showed that at any rate in two hundred and forty-five days such increased freedom has again been contracted to normal limits.

Summary of Results.

Evidence from various sources based on observations of kidneys in various animals from five to three hundred and thirty-nine days after decapsulation conclusively proves that decapsulation of a normal kidney may cause an interstitial nephritis of greater or less extent, varying from a simple invasion of parenchyma with connective-tissue processes in the early cases, to marked and advanced replacement fibrosis, and accompanying degeneration of renal epithelium in the tubules, and, occasionally, even atrophy and destruction of the glomeruli.

There are usually found, sooner or later, after decapsulation, some new blood channels between the kidney and the new capsule, and between the capsule and tissues or organs which may have become adherent. The conditions favorable to this production of new bloodvessels are: an intraperitoneal operation, the injury of adjacent tissues, the formation of natural or induced cicatrices, and a certain length of time after operation. These vessels when formed apparently increase in size and number according to the amount of connective tissue in the adhesions or the capsule to be nourished; they then appear to be gradually compressed with the contraction of the connective tissue, and the greater firmness and denseness of the newly formed capsule, until their number is inconsiderable and their size greatly reduced, so much so as to show no striking differences from the vascular supply found in a normal intact capsule.

The thickness of the new capsule and the abundance of bloodvessels seem to be accompanied in proportion by an increase of the connective-tissue infiltration and by a parenchymatous degeneration of epithelium. When the decapsulation is performed extraperitoneally the vascular new-growth is at its minimum, the interstitial increase in the parenchyma is not noteworthy, and the only evidence of change in the kidney is the contraction of the new fibrous envelope upon the kidney, causing an unevenness of its surface.

The preliminary report of this work made a year ago[6] indicated the results above stated, and I feel now that it is right to say that after decapsulation of a kidney we may hope for a temporary relief from pressure; and if under the proper conditions we may expect an increased vascular supply for a limited period. But we must face the certainty of the formation of a quickly forming, dense, and contracting capsule; the probability of the establishment of a chronic interstitial nephritis in the majority of the cases, and only a possibility of any permanent increase of the renal blood supply.

As a tribute to the successful healing of a severe lesion, such as decapsulation causes, it is fair to state that the newly formed capsule is efficient to protect the kidney from absorption from without, and from extremes of vascular pressure from within. Certainly the possibility of attaining more than a temporary improvement of a diseased condition of a kidney by decapsulation would appear slight.

The theory that an increased vascularization of the kidney formed by the development of contracting scar tissue is able to accomplish a gradual absorption of the interstitial connective tissue among the tubules and glomeruli, thus freeing them from pressure, may be justifiable from the clinician's standpoint, but it has scanty encouragement from experimental research.

Conclusions.—Decapsulation of the kidney in healthy animals may and usually does cause an interstitial nephritis.

New bloodvessels are formed in such adhesions as occur, these vessels being of but temporary character, as they are later occluded by the contraction of the cicatricial tissue surrounding them.

The ultimate result is a newly formed capsule not differing essentially from the original one, except in its tendency to persistent and uneven contraction.

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ON THE EARLY HISTORY OF CEREBRAL LOCALIZATION.

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of Providence.

If we read even superficially the writings of the ancient, mediæval, and early modern physicians I think we will find ourselves asking the question, Why is it that information concerning the nervous system, its anatomy, physiology, and pathology, remained so meagre in comparison with knowledge upon other subjects? Surely there were many instances of nervous disease, and competent observers were not wanting. Sydenham, Harvey, Cullen, the Hunters and Graves, not to mention others, would assuredly have contributed more to our knowledge than they have, were it possible in their age to do so. The explanation of this as of every other phenomenon in the course of thought is to be looked for, I believe, in the intellectual history of the times. Men, for various reasons, were not prepared to understand the nervous system, and among several it would seem that four causes have a special significance: first, an erroneous physiology of the brain; second, the absence of anything approaching to a comprehensive anatomy of the brain, and in particular of its convolutions; third, a speculative philosophy that was content with purely *a priori* explanations of nervous activity; fourth, the lack of an adequate scientific method. To these causes we may, perhaps, add the more general one referred to by Sir William Hamilton, who says: "Of all subjects of scientific interest men in general seem to have weakest curiosity in regard to the functions of their own minds and even bodies. So it is now, and, however marvellous, so it has always been." The influence of each of these factors will appear more plainly as we proceed.

When men began to reflect about themselves and to analyze the content of their consciousness, one of the first results must have been a localization of activity in the various organs of the body; and this is, in fact, what we find. The ancients localized digestion in the alimentary tract, respiration in the lungs, and in a vague general way the intellectual faculties in the brain, although the intimate relation of the thoracic and abdominal organs with the emotional tone of activity often resulted in the reference of mental acts or moral feeling to the heart, the liver, the spleen, or the bowels. Such a tendency may be observed among savage tribes as well as among the more cultured Egyptians and Hebrews, Persians and Arabians, Greeks and Romans. It has been crystallized in language and survives to our own day. We speak of training the heart as well as the mind, and the vagaries of our dyspeptic friend whom we have always with us we ascribe to his liver. With the gradual progress of

anatomy, however, these errors slowly passed away, and the brain came ultimately to be looked upon as the seat of intellect, the centre of sensation, and the source of motion.

When they had confined these functions to the nervous system, philosophers, and with them physicians, who were oftentimes philosophers, propounded the inevitable question, How does the brain exercise its activity? In what manner and by what agency does it think, feel, remember, will, and initiate movement? This leads us to the consideration of a subject which has proved one of the greatest stumbling blocks in the path of progress, and which affords a striking example of the influence of that *a priori* speculative philosophy of which I have spoken. I mean the belief in animal spirits.

In one form or another the theory of animal spirits dominated and obstructed medical thought from Hippocrates to the beginning of the nineteenth century. It is popularly ascribed to Descartes, but its roots reach back to antiquity. Appearing first in ancient medicine as the doctrine of Pneuma—that is, an ethereal principle by means of which the mind performs all the functions of the body—it became the innate heat of Aretæus, and with some modification the Archæus of Helmont and the sensitive soul of Stahl, until finally it survived in a somewhat questionable shape as the *vis medicatrix naturæ* of the school of Cullen. It represented under its various metamorphoses the vitalistic theory of nervous phenomena which has been so energetically opposed by the biochemical explanations of our own day.

The animal spirits were assumed to be a very fine and subtile ethereal fluid elaborated in the brain and used by the soul in the performance of its functions. "Not," observes Galen, "that this animal spirit is of the substance of the soul, but its prime agent while inhabiting the brain." On this point the observations of Dr. Bostock in his *Physiology* are interesting. He says the principal ground for the belief in the existence of animal spirits "seems to have been the idea that the brain is a secretory organ—an idea which was suggested by the great quantity of blood sent to it and by some supposed resemblance in its structure to other secreting glands. Yet as nothing cognizable by the senses is produced by it, it was concluded that it must secrete something of a subtile or ethereal nature peculiarly suited to the performance of the functions which belong to the brain, and which are so unlike those of other material substances. The idea seems to have been originally derived from the alchemists, and, after being incorporated with the metaphysics of the age, gave rise to a long train of mysticism." So firmly was the belief in animal spirits implanted in the minds even of scientific men that John Augustus Unzer, in the latter years of the eighteenth century, writes in his *Principles of Physiology*: "All the phenomena of motion and sensation manifested through the nerves render probable the existence of a remarkably subtile fluid essence which is

present invisibly in the medulla of the brain and nerves, and is the means whereby all the functions of both are performed. It is termed the vital spirit or nervous fluid, but it is not known how and when it contributes to the animal actions." And as late as the first quarter of the nineteenth century we find John Mason Good telling us in his *Study of Medicine* that the brain is a gland producing an ethereal fluid. "As we are justified," he observes, "by all the force of analogy in regarding it (the brain) as a gland, though unquestionably a gland of a peculiar kind, and as we are equally justified on the same ground of analogy in regarding the nervous power or energy by which it maintains a communication with every part of the system as a fluid of a peculiar kind, we are almost driven to the necessity of contemplating it as the source from which this fluid issues and by which it is supplied as it becomes exhausted." Such was the teaching of authority during centuries concerning the brain. Analogy, nothing more, was the slender foundation upon which men reared the superstructure of nervous physiology. The brain was a gland, as even the great Cullen and Malpighi believed; therefore, it must secrete. What? The answer was immediate—animal spirits—about the existence of which the majority of men had no doubt, and about whose nature and activity they talked as glibly as though they had been seen and weighed and measured.

With this explanation of mental life they were content, and so, wrapped about with mists of their own making, they stood still on the road that leads to knowledge; and they advanced, as we shall find, only when the animal spirits had been banished from the high places in nervous physiology.

Erasistratus, Herophilus, Galen, and others of the ancient writers believed in the division of the nerves into those of sensation and those of motion; but it is in the works of Aretæus the Cappadocian, who lived probably in the middle of the second Christian century, that we first find mention of the effect of the position of the lesion upon motion. Treating of paralysis, he observes: "If, therefore, the commencement of the affection be below the head, such as the membranes of the spinal marrow, the parts which are homonymous and connected with it are paralyzed, the right on the right side and the left on the left side; but if the head be primarily affected on the right side the left side of the body will be paralyzed, and the right if on the left side. The cause of this is the interchange in the origins of the nerves, for they do not pass along the same side until their terminations, but each of them passes over to the other side from that of its origin, decussating each other in the form of the letter 'X.' " This, so far as I know, is the first mention in medical literature of the fact that cord lesions affect motion on the same side, while brain lesions produce their symptoms upon the opposite side of the body.

Following Aretæus, cases were recorded by Valsalva, Wepfer, and Morgagni, in which paralysis upon one side of the body was

proven by autopsy to have been due to disease upon the opposite side of the brain, most commonly in the region of the great basal ganglia.

A quaint piece of writing upon this subject has been pointed out to me by Dr. Joseph Sailer, and is to be found in the preface to the edition of *Poor Richard's Almanac* for 1740. The spirit of a rival editor—Leeds—thus describes how he impelled Franklin to write a letter to himself: "Finding you asleep I entered your left nostril, ascended into your brain, found out where the ends of those nerves were fastened that move your right hand and fingers, by the help of which I am now writing unknown to you." It will be observed, he says, he entered the "left nostril," which would lead us to believe that the fact of motor decussation was current knowledge in those days, and that Franklin obtained it from some popular work on physiology. But concerning his idea that the nerves of the hand and fingers terminated in the brain and that the impulse to movement originated in these terminations, I am unable to form any definite conclusion. The eighteenth century physiology certainly taught no specific localization, and Franklin's statement is probably a shrewd guess founded upon the general belief as expressed by Boerhaave, that the nerves run without interruption from the periphery to the brain, and that voluntary motion had its origin somewhere in the cerebrum.

We have seen that the belief in motor decussation was prevalent from the time of Aretæus, but to Gall and Spurzheim must be attributed the credit of the first anatomical demonstration of the crossing of nerve fibres, which takes place in the pyramids. The knowledge of decussation led, however, to no more refined localization of function than that expressed by Haller in his great work, *Elementa Physiologiæ*, published in 1757. There he recognizes in a general way that if the brain be compressed that part of the body is deprived of motion the nerves of which arise from the compressed portion, and this represents the sum of topographical diagnosis until well along in the nineteenth century. As late as 1869 Niemeyer was obliged to say in his text-book: "It is rarely possible to recognize the seat and size of a tumor exactly, but it may be approximately decided in what part it is located, whether in the cerebrum, medulla oblongata, or cerebellum, at the base or convexity. The brilliant diagnoses where the precise localization of a tumor is fully confirmed by autopsy are not usually due to acumen in the observer, but are cases of lucky diagnosis."

I cannot leave this part of my subject without referring to a remarkable conjecture of Nicolaus Stenson, quoted by Sir Michael Foster. Writing in the seventeenth century on the "Anatomy of the Brain," Stenson expresses himself in these words: "If, indeed, the white substance (of the brain) of which I am speaking be, as in most places it seems to be, wholly fibrous in nature, we must neces-

sarily admit that the arrangement of its fibres is made according to some definite pattern, on which, doubtless, depends the diversity of sensations and movements." Here we have a suggestion which, had it been acted upon, would have gone far toward unravelling the truth, but it fell upon ears incapable as yet of understanding it, and so it remained barren of any fruitful consequences.

I wish now to return to the early views concerning the localization of the higher functions of the mind, and I cannot do better than begin with a quotation from the great Frenchman, Trousseau. He says: "You know, gentlemen, that medicine always takes its inspiration from the reigning philosophy, which means that every philosophical doctrine has in the history of medicine a corresponding medical doctrine." If we bear this important truth in mind we will many times discover that the explanation of some otherwise vague medical belief is to be found in the philosophy which underlies it. "The philosopher," says Aristotle, "should end with medicine, the physician commence with philosophy." And as medical thought to-day is prone to follow the naturalistic philosophy of Condillac, Bain and Spencer, just so the older physicians incorporated the fashionable philosophy of the times in their explanations of mental life. Plutarch and Theophrastus tell us of the physician Alcmaeon, believed to have been a contemporary of Pythagoras, who regarded the brain as the common meeting place of the senses. Hippocrates placed the mental faculties in the brain, and in treating of insanity he remarks that a man is sane if his mind is undisturbed. Plato taught that the mind has three distinct faculties, each possessing its separate seat: one, the concupiscent, having its seat in the liver; the second, the irascible, with its seat in the heart; the third, the rational, residing in the brain. He was followed in the course of time by Galen, Vesalius, and others, who, deriving their inspiration from his philosophy, acknowledged three spirits: the natural, passing from the liver with the blood; the vital, flowing from the heart to the body through the arteries, and the animal, distributed from the brain through the nerves. Curiously enough, Aristotle, although the disciple of Plato and the son of a physician, thought the brain a cold and bloodless organ whose function was to cool the ardent heat of the heart, which he regarded as the seat of life, and whence he believed all the nerves to arise. Galen, who exercised a greater influence over medical thought than any other man before or since, opposed the views of Aristotle, and taught that the brain was the organ of mind as well as the centre for all the senses and the source of motion. After Galen, according to Prochraska, the Arabians localized function in the different portions of the brain. One anterior ventricle was supposed to be the seat of common sensation, the other of imagination. In the third ventricle they placed understanding, and in the fourth memory. This was the doctrine of Duns Scotus and of Thomas of Aquin, in

his treatise *On the Powers of the Soul.* It was the classical teaching during the middle ages and early modern times, and is well expressed by Burton in that most curious of books, *The Anatomy of Melancholy.* "This forepart" (of the brain), he says, "hath many concavities distinguished by certain ventricles which are the receptacles of the spirits brought hither by the arteries from the heart, and are there refined to a more heavenly nature to perform the actions of the soul. Of these ventricles there are three—right, left, and middle. The right and left answer to their sight and beget animal spirits; if they be in any way hurt, sense and motion ceaseth. These ventricles, moreover, are held to be the seat of the common sense. The middle ventricle is a common concourse and concavity of them both; in this they place imagination and cogitation, and so the three ventricles of the forepart of the brain are used. The fourth creek behind the head is common to the cerebel or little brain and marrow of the backbone, the last and most solid of all the rest, which receives the animal spirits from the other ventricles and conveys them to the marrow of the back, and is the place where they say the memory is seated." From the foregoing quotation we may well understand what haziness characterized the views of our forefathers. It is true that Vesalius had called such beliefs "reckless opinions," "figments imagined, surely not without grave impiety," but the mind of Vesalius in this, as in so many other things, was far in advance of his age, and the reckless opinions, modified in various ways to suit their fancy or philosophy by Descartes and Willis, continued to rule men's minds to the end of the eighteenth and, indeed, strange as it may seem, found adherents in the early years of the nineteenth century.

As far back as the end of the sixteenth and beginning of the seventeenth century there had been opposition to the view that the ventricles are the manufactory and storehouse of the animal spirits. By the teachings and influence of Caspar Bauhin, Varolius, Spigelius, Hoffman, Caldani, and others the animal spirits together with the higher faculties, such as memory, imagination, and perception, were removed from the ventricles and placed in the solid matter of the brain, while some went so far as to assert that the intellectual functions were entirely independent of the brain and belonged to the immaterial spiritual soul. As men became emancipated from psychological mysticism, and as the new sciences of physics and chemistry came to exert a powerful influence upon thought, the tyranny of the animal spirits was slowly though surely undermined until at last they were dethroned altogether.

In 1784 we find Prochraska writing with a wholly modern tone in his *Dissertation on the Functions of the Nervous System:* "Notwithstanding the authority of these great names (Haller, etc.), the love of truth excited distinguished men, who advanced doubts as to this hypothesis of the animal spirits, and who showed that the argu-

ments adduced in its favor proved nothing when carefully analyzed, and that the whole hypothesis was altogether devoid of truth." He then goes on to say: "We will term the cause latent in the pulp of the nerves, producing its effect and not as yet ascertained, the *vis nervosa;* we will arrange its observed effects, which are the functions of the nervous system, and discover its laws." Here, then, we witness the exit of the animal spirits, which for centuries had held physiology so firmly in their grasp and had so effectually throttled every sort of progress. We have exchanged the transcendental speculations of metaphysics for the demonstrations of physics, and we shall shortly observe the good effects resulting from this removal of the physiological rubbish of antiquity and the placing of physiology upon an assured foundation.

The opinion long prevailed, as we have seen, that certain portions of the brain were connected with definite functions, some with organs of sense and voluntary motion, others with different vital functions. Among the first to point this out definitely was Willis, whose opinion was embraced and zealously defended by the celebrated Boerhaave and many of his disciples. The belief was derived partly from observations and experiments on the effects of injuries to the cerebral hemispheres, and partly from the investigations of comparative anatomy. Prochraska says very definitely, despite the teaching of Haller to the contrary, that it is "by no means improbable that each division of the intellect has its allotted organ in the brain," though he further observes that notwithstanding the labors of many eminent investigators the whole subject was still in obscurity.

The first systematic attempt, however, to localize cerebral function was made during the first quarter of the nineteenth century by the physician, Franz Joseph Gall, and his pupil, Johann Gaspar Spurzheim. The ill-repute into which their system has justly fallen has detracted from their real merit as scientific investigators. As a matter of fact, they were among the most eminent men of their time, their contributions to anatomy are valuable, and it was Gall who, by dissecting the brain-stem from below upward, inaugurated the method which was subsequently to produce such notable results.

These two physicians elaborated a "physiognomical system" which, under the name of phrenology, attracted a larger share of attention than its real merits justified. Gall divided the skull into twenty-six and Spurzheim into thirty-five regions, each supposed to represent the organ of some particular mental aptitude.

While it is now universally recognized that at the time of its promulgation phrenology was premature, being incorrect both in localization and in the psychological analysis of the mind, still it had the great merit of provoking severe criticism, which was, unfortunately, often extremely personal, and thus of drawing attention to the whole subject. Although discredited itself, one of its important

results was that from the time of Gall and Spurzheim the tendency has always been more strongly toward a topographical localization of mental activity.

I have mentioned as one of the causes contributing to the backward state of neurological knowledge the absence of an adequate scientific method. Until the introduction of the inductive method as propounded by Bacon and further elaborated by Newton, Locke, and later by Hume and John Stuart Mill, there was no possibility of verifying and controlling hypothesis by fact, and, especially in the domain of the nervous system, no means of advancing from the known to the unknown. But with the advent of physiological experimentation the aspect of things was changed. The illustrious Haller was among the first of physiologists to employ this method in his work. "As the nature of the brain and of the nerves is one and the same," he says, "so are these alike in function. In treating of them we will so far as possible make use of experiments, nor will we at first at least go beyond the testimony of our senses." And if we wish to observe what a revolution the new method wrought we have only to compare the mystic Swedenborg's *Œconomia Regni Animalis*, published in the middle of the eighteenth century with Haller's *Elementa Physiologiæ*, published a few years later. By means of experiment, first, Magendie, in 1822, and later Sir Charles Bell discovered that the anterior spinal roots are motor and the posterior sensory in function, thus beginning a new era in nervous physiology and laying the foundation of the subsequent progress, which has continued without pause to our own day.

In the reaction following the teaching of Gall and Spurzheim, whose conclusions went far beyond the facts, the pendulum had swung to the opposite extreme, and from the experiments of Magendie, Longet, and in particular of Flourens, special localization of function in the cortex was discarded and the classical physiology taught, even against the strongest evidence to the contrary, the equivalence of mental function, that is, the brain as a whole, not any definite portion, was considered to be the physical substratum of mental activity.

The work of Flourens corroborated the previous experiments of Molinelli, Rolando, Krauss, Hertwig, and others, and was itself corroborated by the later researches of Serres and Desmoulins. The theory received the sanction of the celebrated Cuvier, and so convincing apparently was the evidence upon which it was founded that it formed the belief of the ablest physiologists down to the present period, which began in reality in 1822, but which attained no special influence until 1861.

But before considering the question of aphasia I wish to preface a word concerning the anatomy of the cerebral convolutions. The earlier physicians were surprisingly ignorant of the anatomy of the

hemispheres, and in this connection there is an interesting paragraph in the work on *Apoplexy* and *Lethargy*, written by the celebrated Cheyne, of Edinburgh, and published in 1812. "Our knowledge of the brain," he observes, "is still circumscribed within very narrow bounds; we do not know with certainty anything beyond the form, consistence, and color of its various eminences, depressions, and cavities, and the origins of the nerves and distribution of the bloodvessels which connect this organ with the rest of the system. We, indeed, know from the effects of similar diseases of the brain that sensation and volition are functions of this organ, but we are as much in the dark with regard to the use of most of its parts, its ultimate structure, and the kind of influence which it exerts over the body and most of the circumstances upon which the origin and transmission of that influence depend as we are with respect to the nature of the impressions made by external objects upon our organs of sense, or the sensations associated with those impressions." A part of the ignorance of which Cheyne speaks was certainly due to the beliefs in vogue concerning the cerebral convolutions. Their arrangement was thought to be purely a matter of chance, and in the older records of cases of brain disease we usually find the position of the lesion roughly described as being in the anterior, middle, or posterior lobe. It remained for Leuret and Gratiolet to demonstrate clearly that there was an orderly plan in the convolutions, which could be traced from the inferior mammals, through the monkey up to man. The researches of these great observers, and especially of their successors, Ecker, Broca, and Gromier, by mapping out for us the morphology of the external surface of the brain, removed the chief anatomical obstacle that I have mentioned, and made it possible for us to describe accurately the precise location of any lesion. The scholarly little work of Ecker on *The Convolutions of the Human Brain* and that of Gromier entitled a *Study upon Cerebral Convolutions in Man and Monkey* did much to lead men out of the labyrinth of error, where it was customary "to regard the convolutions as a series of folds without order or arrangement, and draughtsmen represented them much as they would a dishful of macaroni."

It is commonly stated that the first case in which the loss of articulate speech was attributed to a lesion in the left frontal lobe was reported by Thomas Hood in 1822. This, however, is not historically accurate. There is a case detailed by Pourfour Petit in 1766 which represents probably the first case in medical literature. It is recorded by Austin Flint in his *Physiology of Man*, from which I have taken it. Writing in his *Nouveau système du cerveau* Petit says: "Some time after I had made the experiments which I have just reported a cavalryman of the garrison, aged thirty-five years, was brought into our hospital. He had been seized the day before

with paralysis of the entire right side, which had occurred after a slight pleurisy, from which he had recovered. He could move neither the arm nor the right leg, nor could he maintain himself in his seat. The lower jaw was not distorted. He opened and closed the mouth with facility. He could move the tongue only with great difficulty, and could not protrude it from the mouth, nor pronounce any word. He retained sensation on the paralyzed side. A month after he had entered the hospital he moved the tongue pretty easily, and even protruded it a little from the mouth, but he could pronounce nothing but "Non." After death I removed the brain and spinal cord. I began by dissecting the spinal cord, in which I found nothing abnormal, nor in the right side of the brain. But I found on the left side the entire anterior protuberance which contains the internal and superior corpora striata, the middle and the external or inferior, dissolved and converted into a substance resembling the lees of wine. It did not appear that this part had been swollen and that it had become larger than natural. Neither the optic thalami nor the optic nerves were injured."

From this most interesting case of Petit nothing was written concerning aphasia until 1822, when the English physician, Thomas Hood, recognized that disturbance of speech was caused by a lesion affecting the frontal lobes of the brain. In 1825 Bouillaud, in France, as the result of experimentation and clinical experience, maintained that a lesion in the anterior lobes causes loss of speech, and he further believed in the existence of cerebral motor centres, destruction of which causes localized paralysis. In a paper read before the Medical Congress at Montpellier in 1836 Marc Dax reported impairment or loss of speech in 140 cases of right hemiplegia, from which he concluded that the faculty of articulate language is situated in the left anterior lobe. However important were these observations in pointing the way, it is to Paul Broca that we owe the definite localization of the speech centre. In 1861 Broca, as the result of clinical observation, placed it in the third left frontal convolution, and in the heated discussion on aphasia at the Academy of Medicine at Paris, in 1864, further light was thrown upon the subject, the conclusions of Broca were confirmed, and thus, after the lapse of centuries, we behold the first absolutely definite localization of function in the cerebral cortex. Following Broca's dramatic and truly epoch-making discovery, came the observations of Hughlings Jackson on localized epileptiform convulsions, those of Aubertin, Charcot, Pitres, Falret, Trousseau, Séguin, Bastian, Broadbent, Wernicke, Kussmaul, Fritsch and Hitzig, and a host of others whose labors have pointed the way from haziness to definite scientific conceptions. They are the pioneers who have laid the foundations of neurology broad and sure. And, based largely upon their labors, neurology has gone forward, often it is true, with halting

steps, but none the less forward, until to-day it possesses a body of assured truth upon which we daily levy tribute in our battle with disease.

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REVIEWS.

Subjective Sensations of Sight and Sound, Abiotrophy, and Other Lectures. By Sir William R. Gowers, M.D., F.R.C.P., F.R.S. Philadelphia: P. Blakiston's Son & Co., 1904.

This compact volume of 250 pages is a presentation in lecture form of a variety of subjects mainly pertaining to neurology. The first of the articles, that on subjective visual sensations, an address to the Ophthalmological Society of London, is an excellent presentation of various visual phenomena seldom written of and little understood. In explaining the relation of the visual sensations to the functions of the cerebral cortex he invokes the aid of the visual disturbances of hysteria, reversing his own previous attitude, and places the subject in such a state that a careful neurologist or ophthalmologist will find no little intellectual exercise in straightening out the tangle of argument. The study of color-vision and the visual fields, the subjective visual sensations of migraine and epilepsy, all of which are used in his explanation of the relation of peripheral and central vision, are, apart from this, valuable contributions to the subject and interesting reading.

Subjective sensations of sound are treated in a similar, if less complex, way.

The need for a comprehensive term to designate a large group of diseases affecting the nervous and muscular systems dependent on an inherent lack of vitality, or working ability, has long been felt. In the third lecture Gowers proposes the term "abiotrophy" to supply this want, and the term has obtained general use among neurologists in a very short time. The adjective abiotic, while strictly correct, is somewhat foreign in sound to abiotrophy, and a tendency has been manifested to use the term "abiotrophic" in its place in case-records, etc. The explanation and discussion of various forms of abiotrophy—the muscular dystrophies, etc.—is presented in the following lectures.

The effects of lead and arsenic on the nervous system are considered in separate lectures. In the remaining lectures syphilis of the nervous system, syringomyelia, and the use of drugs are treated. All of the articles are valuable contributions to their respective subjects. Gowers has set an example for those of wide experience and sane judgment in correlating isolated facts and

sifting the evidence concerning various subjects and presenting them in book form in an authoritative way. As parts of a book the individual articles have an added value on account of their permanency, and because the author—than whom there is no better judge of what is of value in neurological literature—considers them worthy of being so placed. D. J. McC.

THE THERAPEUTICS OF MINERAL SPRINGS AND CLIMATES. By I. BURNEY YEO, M.D., F.R.C.P., Emeritus Professor of Medicine in King's College, London; Consulting Physician to King's College Hospital, etc. Pp. 760. Chicago: W. T. Keener & Co., 1904.

WE welcome this volume, which suggests the author's *Climate and Health Resorts* as its foundation, but which, based upon a larger and riper experience, brings us to the present. With the increased attention of late given to physical measures for the restoration of health comes added interest in the subject, so that this book is timely and important. With the knowledge shown in other works, this broader view cannot but be of advantage to the reader. Of the first part—mineral springs—much has been written from the viewpoint of this exploitation, through an effort to obtain a scientific explanation of varying therapeutic effects when chemical analysis shows minute differences in constitution, to serious attempts to place a fair statement as to what conditions, and more particularly, what patients are likely to be benefited. From the patient's standpoint this book has been written, even if the difficulties of the "indifferent springs" have not been fully elucidated. Of the topics presented, the nature, composition, and classification of the springs, modes of application, action, accessory method, lead to the description of the principal springs, which are considered alphabetically. The application of mineral water and baths complete the subject. If criticism of an excellent book be not unkind we would suggest that, in addition to those considered, there are some which have been omitted, and that perspective as shown in the use of smaller type is not always in accord with importance. As to the second part—Climate and Climatic Resorts—the divisions embrace climate and climates, sea or mountain, seaside and mountain resorts, winter quarters, the Western Riviera, sea voyages, and, finally, the practical portion —the application and selection of climates and treatment in sanatoria, which includes a list of the same. The places mentioned are such as, in the judgment of the writer, "are fairly accessible to and likely to be visited by English invalids." Here, again, we except to the author's limitation of the globe-trotting propen-

sities of our English cousins, and believe that many places not here mentioned have a climate, not weather, of which he might hear somewhat favorably from his professional brethren. Not that we believe that what our country possesses needs consideration, much less eulogy, but now that our own authors have presented volumes of no mean reputation, a complete guide cannot be predicated unless these volumes have been consulted. To be sure, we find mentioned many resorts of household reputation, but too briefly for accurate judgment as to their value. As a book for consultation, if not so complete, yet more readable than an assemblage of official reports with which we are familiar, as a fair statement of well-ascertained facts, as a book of attractive presentation, bearing the impress of the author's personality, we give this a prominent place in our library.

R. W. W.

A Practical Treatise on Nervous Diseases for the Medical Student and General Practitioner. By F. Savary Pearce, M.D. New York and London: D. Appleton & Co., 1904.

Both Gowers and Oppenheim have well demonstrated that it is not at all necessary to differentiate the student or general practitioner from the skilled neurologist in presenting the subject under consideration. With such standards of excellence in book writing, the assertion in the title of a new work that it is primarily intended for the student and general practitioner should not protect it from criticism or from comparison with what is best in neurological literature. Were the book intended for the students of the institution of which the author was professor of neurology it would undoubtedly fill a distinct want, were it followed in preventing a confusion of such ideas as are frequently presented with that of established teaching. Beyond such a scope of influence, in the hands of the general practitioner, it would do harm as an inaccurate presentation of an important subject. To teach that "paresis" of the third nerve produces nystagmus, protrusion of the eyeball, and ptosis" is, to say the least of it, misleading. Many such misstatements might be quoted.

The general arrangement of the subject-matter and its form of presentation is good; the English is, however, complex, compressed, and very often with difficulty understood.

The real value of the work lies in the large number of well-executed illustrations, which are, on the whole, appropriate and pertinent to the subjects illustrated, and are here permanently placed on record as a real addition to the subject of neurology.

The book cannot be recommended to the student or the general practitioner, for whom it was intended, but should be in the hands

of every specialist of the subject—every specialist who has written or intends writing a book. To such it will have a peculiar and personal value. M.

ATLAS AND EPITOME OF OPERATIVE GYNECOLOGY. By DR. OSKAR SCHAEFFER. Edited by J. CLARENCE WEBSTER, M.D. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

As stated by the author in his preface, the difficulties of demonstrating the various operations of gynecology, particularly the different modes of attack by the vaginal route, are probably greater than in any other province of surgery. To meet this difficulty is the object of the present volume. When one considers the inherent difficulties of the attempt only praise can be felt for the way in which the artist has fulfilled his part.

As to the gynecological teaching, there is much that might be criticised, as, for instance, the recommendation of Hegar's perineorrhaphy, the including of hysterocleisis, and colpocleisis and the vaginal fixation of the uterus.. We believe that the book will, however, if used as intended by the author, in conjunction with a good clinical course, serve a useful purpose. W. R. N.

DISEASES OF THE NERVOUS SYSTEM: A TEXT-BOOK FOR STUDENTS AND PRACTITIONERS. By H. OPPENHEIM, M.D. Translated and edited by EDWARD E. MOYER, A.M., M.D. Second American edition. Philadelphia: J. B. Lippincott Co., 1904.

THIS new edition of the most popular of the German text-books follows close on the third German edition. The plan of the German edition is closely followed, and additions are made only when it is necessary to elucidate some obscure point or to give credit to American investigators. For clearness of conception, consideration of material, scientific accuracy, and thorough treatment, the German edition finds no equal, either in nervous diseases or other fields of medicine. The book has lost none of these qualities in the translation, but in an attempt at a literal translation of the German text the English construction is frequently awkward and clumsy. There is little excuse for this, as our own language is much better adapted for purposes of condensation of material than is the German. The improvement over the preceding edition is evident in the number of illustrations of disease types and of pathological specimens. There is no other work so well illustrated, nor is there any to which the illustrations are of so much value in elucidating

the text. They impress one as an essential element of the work, and not merely, as is so often the case, as added pictures to attract the eye.

Much has been added to the treatment of the functional nervous disorders, but not from an American standpoint. Fifteen pages of treatment are given for neurasthenia and hysteria, with the Weir Mitchell rest treatment relegated to a small paragraph of fine print of less than one-fourth of a page.

To those who are unable to read the original German edition the English translation can be recommended as one of the best text-books on the subject. D. J. McC.

Les Maladies de l'Estomac. Paris: J. Rueff, Editeur, 1904.

This royal octavo of about 1200 pages presents, in addition to the clinical experience and therapeutic teaching of the author for fourteen years past at the "Hôpital de la Petit," an admirable and exhaustive review of the work of the leading specialists in this field throughout the world. Briefly stated, the book is divided into five parts, viz.: first, clinical and physical examination of the stomach and contents; second, dyspepsias, general considerations, treatment, nosology, prophylaxis, symptomatology; nervous, alimentary, and reflex types and the treatment thereof; changes in urine and blood occurring therein; pyloric stenoses, gastric fermentations, hydrotherapy; third, organic maladies of the stomach, etiology, pathology, and treatment; fourth, pathogenic role of stomach affections in relation to other organs and their functions; fifth, the reaction of other maladies on the stomach. This work is thorough, and presents the views of the leading authorities and specialists throughout the world, the German authorities, as usual, leading in the number of references, although French and American authors are quite copiously quoted. All in all, this volume will compare very favorably if, indeed, it will not surpass, any similar work issued to date. E. A. H.

Vaginal Tumors, with Special Reference to Cancer and Sarcoma. By W. Roger Williams. London: John Bell, Sons & Danielsson, 1904.

This very valuable book, small in size, but covering its ground very fully, is to be recommended to all who are interested in neoplastic vaginal formations. While the subjects considered are not among the most frequent to be met with in a medical practice, yet

the great importance which they assume is sufficient excuse for the appearance of this admirable volume.

While the scientific side of the question, namely, the etiology of the genesis of these formations, is not slighted, the book is replete with the practical details and, as the author claims in his preface, has the great recommendation of conciseness. There are five chapters, the first two being devoted to cancer and sarcoma; the third and fourth to non-malignant growths, as myoma, neuroma, etc., while the last deals with the very interesting cystic formations.

W. R. N.

PORTFOLIO OF DERMOCHROMES. By PROFESSOR JACOBI, of Freiburg, in Breisgau. English adaptation of text by J. J. PRINGLE, M.B., F.R.C.P., Physician to the Department for Diseases of the Skin at the Middlesex Hospital, London. Vol. II. New York: Rebman & Co., 1903.

THE high standard of excellence reached in the first volume of Jacobi's *Atlas of Diseases of the Skin* is well maintained in the second and concluding one. Many of the portraits leave little to be desired in the way of accurate and lifelike representations of diseases of the skin.

This volume of the *Atlas* contains forty-four plates, of which fifteen are devoted to cutaneous syphilis. We note with hearty approval that the author has thought worth while to give some space to the subject of drug eruptions—an important subject from many points of view to which not enough attention is paid. Six plates are given to the lesions which result from the internal use of the iodides, the bromides, antipyrin, arsenic, and copaiba. An especially interesting portrait is the one representing arsenical hyperkeratosis of the palm, not only because it is a truthful representation of this form of keratosis, but because of its importance as an occasional forerunner of epithelioma. The eleven portraits of the various forms of eczema are among the very best we have ever seen, the plate representing eczema madidans being wonderfully lifelike.

As in the first volume, the text is extremely condensed, being limited to the briefest consideration of the etiology, diagnosis, prognosis, and treatment of the diseases illustrated. In the endeavor to be brief matters of some importance are occasionally overlooked, as when no mention is made of the fact that pemphigus neonatorum is almost certainly identical with impetigo contagiosa, and may prove fatal in very young infants.

In conclusion, we have no hesitation in saying we believe this to be one of the very best atlases of diseases of the skin yet published.

M. B. H.

THE EYE, ITS REFRACTION AND DISEASES: THE REFRACTION AND FUNCTIONAL TESTING OF THE EYE, COMPLETE IN ITSELF. In twenty-eight chapters, with numerous explanatory cuts and diagrams. By EDWARD E. GIBBONS, M.D., Assistant Surgeon to the Presbyterian Eye, Ear, and Throat Hospital; Demonstrator and Chief of Clinic of Eye and Ear Diseases in the University of Maryland, Baltimore. New York and London: The Macmillan Co., Ltd., 1904.

THE beginnings of the chapters of this book open up an attractive outlook. Certain subjects are here brought together not accessible, as a rule, in the ordinary text-books. The writer makes free use of elementary formulæ in his treatment of ophthalmic optics. We regret to have to note a number of inaccuracies which are likely to prove stumbling blocks to the student. The printer's part in the work is most excellent, and will no doubt prove a valuable adjunct in the sale of the book. T. B. S.

PHYSICAL TRAINING FOR WOMEN BY JAPANESE METHODS (JIU-JITSU). By H. IRVING HANCOCK. New York and London: "The Knickerbocker Press," G. P. Putnam's Sons, 1904.

JIU-JITSU gives the average American woman an entirely new view of her Japanese sister—it seems almost impossible to believe that they are so much in advance of a race of women to whom systematic exercise is a threadworn subject.

The author has illustrated his book profusely, and the text is most concise, but the great drawback to the practicability of the method is the fact that it requires two persons to carry out most of the exercises. The exercises for developing the "chest and the hollow between the shoulders" are particularly good, and can be done by any woman at home. The chapters on "Our Outdoor Sports for Women" and "Sleep and Its Value" are full of suggestions that are worthy of a trial at least. Some attention has been given to "obesity and leanness," but nothing particularly new is advised.

On the whole, the book is very interesting, and the methods carried out in a regularly organized class would undoubtedly prove of great value to the students, but as a guide for the individual it is of little use, as only two or three of the exercises can be done alone; there must be an "assailant" and a "victim" to carry out the methods of "jiu-jitsu" successfully. W. R. N.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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Primary Endothelioma of the Pleura.—PAUL BONHEIM (*Münch. med. Wochenschr.*, 1904, li. p. 741) reports three cases of primary endothelioma of the pleura, and discusses the diagnosis and pathology. The first case, a man, aged fifty years, was treated for three months for left-sided pleural effusion, a clear serous fluid being obtained by puncture. A month later a litre of clear fluid was again withdrawn. After a week he re-entered the hospital on account of dyspnœa and continuous pain in the side. He was much emaciated; hæmoglobin, 60 per cent. The left side showed evident signs of fluid, but the lower costal spaces of the lateral chest wall were shrunken. The first aspiration again yielded clear, serous fluid, but the second was markedly hemorrhagic. The patient suffered most intense pain in the side, controlled only by morphine. Death occurred suddenly six months after the beginning of treatment. The anatomical diagnosis was right-sided adhesive pleurisy; hemorrhagic exudate on the left, the pleura being covered with a thick fibroid exudate; compression and chronic pneumonia of the left lung; embolism of right pulmonary artery. Microscopically, sections of the pleura showed a dense network of connective-tissue fibrils with few spindle-shaped nuclei, and scattered through this groundwork numerous anastomosing, long, round tubules lined with cubical epithelial cells, in places arranged in several layers. The deeper layer of the exudate was composed of a less cellular connective tissue with round-cell infiltration and only an occasional tubule.

The second case, a man, aged fifty-five years, complained of pain in left side and dyspnœa. There were evident signs of fluid in the left pleural cavity, and clear serum was obtained on puncture. He was tapped in all six times, the fluid after the first puncture being markedly hemorrhagic. The chest was aspirated on account of the rapid return of the fluid and of the dyspnœa, and two ribs were finally resected a

month after entry. The pleura was thickened and covered with small prominent, shining nodules, which were regarded as tubercles. The microscopic report, however, showed an excised piece to consist of an intercommunicating system of tubules lined with low epithelioid cells. The patient died three and one-half months after the operation. The autopsy showed endothelioma of left pleura, with metastases in the lungs, glands, spleen, liver, and adrenals.

The third case was that of a Chinaman, aged thirty years, who was admitted with symptoms of a severe left-sided exudative pleurisy, and rapidly died of cardiac weakness. The condition of the pleura was found to be the same as in the other cases.

All cases reported in literature have presented a microscopic picture similar to that observed in these three instances. Macroscopically, two forms may be distinguished: 1. A diffuse, uniform thickening resembling, even at autopsy, an ordinary fibroid pleurisy as in Case I. 2. More commonly the thickened pleura is studded with small cartilaginoid projections.

Cases of pleural endothelioma run their course under the picture of hemorrhagic pleuritis, but there are certain symptoms which should direct attention to the condition. The diagnosis has been made *intra vitam*. A clear, serous fluid on the first tapping, becoming blood-tinged later, and then more and more hemorrhagic until it has a deep chocolate-color, is very suggestive. This condition has been noted in nearly all reported cases. The fluid reaccumulates rapidly, and, as Podack remarks, each successive puncture gives less and less relief. Finally, the heart becomes fixed in its displaced position and does not recede after the fluid has been withdrawn. Of course, the primary step is to exclude tuberculosis and secondary carcinoma. Podack demonstrated clumps of tumor cells in the exudate from his case, but this would be no constant finding. Fraenkel has pointed out as characteristic the retraction of the lower intercostal spaces in spite of the presence of a large amount of fluid, and Bonheim emphasizes the very evident progressive retraction of the whole side of the chest. This was strikingly present in the first case. The reported cases have been almost exclusively in males, and the left side has usually been affected. In regard to the pathology of these tumors, Benda was able to demonstrate their growth from the pleural endothelium, and Podack from the lymph spaces. Numerous names have been suggested for the condition: carcinoma, endothelial carcinoma, lymphangitis carcinomatodes, lymphangitis proliferans, alveolar endothelial sarcoma. Bonheim thinks the term endothelioma is preferable in that it conveys no false impression.

Blood-pressure Estimations in Arteriosclerosis.—Keigi Sawada (*Deutsche med. Wochenschr.*, 1904, p. 425). The maximum systolic pressure was taken with the Riva-Rocci instrument, as modified by v. Recklinghausen, a firm cuff 15 cm. wide being substituted for the original narrow one. The pressure readings were made after the patients had quietly rested for from a half to one hour in the polyclinic, and after lying down fifteen minutes with the arm band in position. Recklinghausen and Miller give the normal maximum systolic pressure at from 105 mm. to 115 mm. mercury. In a large number of readings Sawada found variations from 90 mm. to 120 mm. Pressure over

130 mm. he considers increased, from 120 mm. to 129 mm. not definitely increased, and below 120 mm. normal.

Of 98 cases of arteriosclerosis in which the heart and kidneys were apparently perfectly normal, in 83 the pressure was normal, in 5 increased, and in 10 not definitely increased. The highest pressure in any case was 176 mm. He divides these cases into three classes: (1) arteries just palpable; (2) arteries distinctly thickened, and (3) actual "goose-neck" arteries. Of 42 cases in the first class, 2 showed increased pressure and 3 pressure not definitely increased; of 42 in the second class, 2 showed increased pressure and 5 pressure not definitely increased; of 14 cases in the third class, 1 showed increased pressure and 2 pressure not definitely increased. The elevation in all but 1 case was slight, and, accepting with Hensen 20 mm. of mercury as the amount of pressure necessary to obliterate the rigid arterial wall alone, most of the figures would be reduced to high normals. Of 206 cases of arteriosclerosis examined, there were 24 with accentuated second aortic sound without any evidence of kidney disease—13 with normal pressure, 10 with increased pressure, and 1 border-line case. Sawada believes that the accentuation of the second sound must be due to factors other than simply increased pressure, as had been previously pointed out by Curschmann. Of 43 cases of arteriosclerosis associated with cardiac insufficiency, in 28 the pressure was normal, in 10 increased, in 5 not definitely increased. In 10 arteriosclerotics with small granular kidneys all showed a marked increase in tension, ranging from 150 mm. to 205 mm. In 4 cases it was over 180 mm. In cases of simple arteriosclerosis Sawada has never observed pressures over 170 mm., except in 1 doubtful case. In 22 further cases associated with albuminuria—excluding those which were recognized as interstitial nephritis—the pressure was normal in 15, increased in 3, not definitely increased in 4. The highest pressure was 148 mm.; 8 of his cases belong to the interesting group occurring, without apparent cause, in children and young adults from fourteen to twenty-six years of age. In 3 of these cases the pressure was over 120 mm., reaching in one 131 mm.

To summarize: 12.3 per cent. of the cases examined showed an increased blood pressure, usually within 130 mm. to 160 mm. Two-thirds of the cases with increased tension were associated with an accentuated second aortic tone. However, there was more frequently an accentuated second aortic without increase in tension. A constant blood pressure over 170 mm. suggests the existence of a chronic interstitial nephritis, even if albumin be absent from the urine.

The Significance of Traces of Blood in the Feces.—Dr. L. Joachim (*Berl. klin. Wochenschr.*, 1904, xli. 466). The chemical investigation of the feces to discover minute traces of blood has attracted considerable attention in the past few years as an aid in the diagnosis of certain diseases of the alimentary canal. Joachim has investigated the condition in a large number of patients to ascertain what reliable conclusions can be drawn from it. He has used both the guaiacum test of Weber and the aloin of Rossel. He finds the aloin test the more delicate of the two, but each has some advantage over the other, and he recommends using both in doubtful cases. In patients suffering with no disease that might explain the presence of blood in the stools the tests

were invariably negative, except in several instances in which they had eaten articles of food containing blood. After slight nose-bleed the tests were positive; after hæmoptysis usually negative, as little sputum is swallowed. In pneumonia blood was never found in the feces. In carcinoma of the stomach blood was missed in the feces in only a single instance out of nineteen. The amount of blood in most instances was very small, but it was constantly present—at least in no case was the stool free from blood for several successive days. Out of twenty-eight cases of gastric ulcer blood was discovered in the stools of twenty-three, not, however, constantly in small amounts, as in the case of carcinoma, but in relatively large quantities, varying with longer or shorter blood-free periods. The hemorrhages bore no apparent relation to the ingestion of solid food. In a large number of cases with tuberculous ulceration of the intestines blood was never demonstrated in the stools. Out of six cases of typhoid fever the tests were positive in two; in one of these the stools showed a positive reaction the day before the onset of a severe intestinal hemorrhage. Boas has observed such "premonitory" traces of blood in cases of gastric ulcer. In a case of mercurial poisoning the tests were constantly positive. They were uniformly negative in cases of gastric catarrh, gastroptosis, intestinal parasites—excepting one case of Balantidium coli—and in lesions of the neighborhood of the intestinal canal, as appendicitis, subphrenic abscess, etc. In cases of general passive congestion, as in broken cardiac compensation, blood was repeatedly found, while in a number of cases of cirrhosis of the liver with portal stasis it is remarkable to note that it was absent. In a case of catarrhal jaundice blood was unexpectedly found on several occasions at the height of the disease, while in several cases of cholelithiasis the tests were constantly negative. A carcinoma of the pancreas gave negative results; a hemorrhagic pancreatitis positive.

Joachim was able to demonstrate traces of blood in the stools of healthy persons after the ingestion of only 3 g. of blood. The chemical tests are much more delicate than the spectroscopic.

While this method of searching for minute quantities of blood in the stools may be very helpful in certain cases, the conditions which may lead to intestinal hemorrhage are so numerous that its value is greatly impaired. As sources of error the author mentions hemorrhoids, menstruation, hemorrhages from the gums and nose, hæmoptysis, and the ingestion of articles of food containing blood. Tests after eating well-cooked meat were negative.

The Value of Jousset's Inoskopy.—E. Körmöczi and K. Jassniger (*Deutsche med. Wochenschr.*, 1904, xxx. p. 342) say that, in order to discover the presence of a very small number of tubercle bacilli in a large amount of exudate, Jousset has introduced a method which he calls inoskopy, consisting in digesting with pepsin the coagulum which forms after the fluid has been allowed to stand, centrifugalizing the digested mass and examining the sediment. Using this method, he reports interesting and surprising results. In 17 cases of pleurisy with effusion, without apparent pulmonary lesions, he found tubercle bacilli in all. In 12 cases of ascites he demonstrated them in 3, although in none of these cases had the diagnosis of tuberculous peritonitis been made. In 2 cases of apparent typhoid fever Jousset established the diagnosis of acute miliary tuberculosis by obtaining tubercle bacilli from

the blood. In 10 cases of chronic pulmonary tuberculosis he found tubercle bacilli in the blood of 2, both complicated with renal tuberculosis, and describes a transient "bacillémie" associated with symptoms of a febrile gastric disturbance, the bacilli disappearing from the blood with the abatement of the symptoms. Following closely the description of the method as given by Jousset, Körmöczi and Jassniger obtained positive results in 3 out of 8 cases of pleuritic effusion. Two cases of ascites were negative, and the heart's blood obtained at autopsy from cases of acute miliary tuberculosis, positive once and doubtful once out of 4 cases. All of the cases examined were definitely tuberculous, and in view of so many negative results they believe that the value of Jousset's method has been overestimated. As possible sources of error they lay emphasis on small scratches on the slides which retain the fuchsin stain and easily deceive unless great caution is used. Small rents in the film and particles of the fuchsin stain which resist decolorization may present figures very similar to isolated tubercle bacilli. The most deceptive pictures occur in connection with the blood coagula, in which are always present masses of small red rods, shorter and thicker than the true tubercle bacilli. The more thoroughly the coagulum is washed the less numerous are these figures, which Körmöczi and Jassniger refer to crystalline particles of blood-coloring matter.

THERAPEUTICS.

UNDER THE CHARGE OF

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Mercurial Inunctions in Syphilis.—Dr. Gailleton describes the most approved form of this classical treatment thus: At each inunction from 1 to 1.5 drachms of mercurial ointment are used and rubbed well into the skin for ten minutes; then gauze or linen is laid over the part. The next morning the skin is bathed with water and a powder of equal parts of soap and sulphur. Each inunction should be made in a different place, the insides of the arms and thighs, the sides of the thorax and abdomen, the folds of the buttocks, the popliteal spaces, axillæ, the hairy region of the pubes, the palms and soles being successively used. The author advises one inunction daily for twenty days, a rest of four days, and a resumption every two days for ten to twenty days. The results achieved will show whether a second like series is necessary. The condition of the kidneys, of the digestive tract, and of the mouth must be carefully watched, the latter being frequently cleansed by antiseptic washes. Patients with irritable and tender skins often cannot endure this form of treatment. Inunctions are especially indicated in grave syphilis at all periods and in rebellious syphilides of the secondary tertiary stage. When mixed treatment is given, potassium iodide is prescribed in connection with the inunctions. The treatment by friction

is contraindicated in pustuloerosive syphilides and other conditions where there are raw surfaces giving an opportunity for absorption.—*Journal de médecine de Paris*, 1904, No. 15, p. 148.

Iodipin.—Dr. M. Fränkel states that this substance is a combination of iodine with oil of sesamum. It is furnished in two strengths of 10 per cent. and 25 per cent. of iodine, respectively. It is a clear, yellow, oily fluid, smelling and tasting like oil of sesamum. The author has used the 10 per cent. iodipin internally in cases of secondary and tertiary syphilis, and has never seen resulting symptoms of iodism, one patient in particular receiving during the course of four to five months over 60 ounces of the substance without untoward symptoms, and with the result of bettering his general condition and increasing his weight. Potassium iodide previously had caused coryza and acne. In chronic bronchitis with asthmatic attacks, the use of iodipin is recommended. Subcutaneous injections of the 25 per cent. strength, in doses of 0.5 ounce or more daily, achieve good results in tertiary syphilis and are attended by no symptoms of iodism. The author reports a case of beginning tabes dorsalis, in which the use of iodipin seemed to have caused a disappearance of the symptoms and to have stopped the progress of the disease. As an injection into syphilitic abscesses and broken-down gummata, iodipin is useful.—*Wiener klinische therapeutische Wochenschrift*, 1904, No. 15, p. 432.

Lumbar Puncture in Ear Lesions.—M. Lumineau has studied the effect of lumbar puncture in various aural disorders, such as affections of the labyrinth, otitic scleroses, dry and cicatricial otitis, and has concluded that aural vertigo, especially when accompanied by Ménière's syndrome, is the symptom most amenable to treatment by this means. Simple labyrinthitis receives the greatest benefit from this treatment, and no other means seems to relieve the condition as effectually. Labyrinthitis with vertigo, with subjective sounds, and the mental state which results from these is also modified by this treatment. The vertigo disappears, the mental condition becomes normal, and the auditory disturbances tend toward disappearance. These troubles are most likely to be ameliorated if they are sequelæ of old suppurative conditions. After dry otitis the results of puncture are less favorable. However, in all aural lesions where other treatment has proved ineffectual, lumbar puncture is worth trying and may be followed by success.—*Revue française de médecine et de chirurgie*, 1903, No. 6, p. 137.

Fersan.—Dr. B. Ehrmann makes the following report upon this preparation of iron and phosphorus. It is prepared from the blood of cattle, 1 per cent. salt solution, and concentrated hydrochloric acid, and when ready for administration is an acid albuminate containing iron and phosphorus, and is in the form of a powder. In proper cases in from ten to twenty days it causes the hæmoglobin to increase 20 to 30 per cent. (Fleischl) and produces a corresponding increase in the red blood cells. The usual dosage is from 4 to 5 drachms per day in divided doses. It is especially indicated in anæmia, chlorosis, convalescence, febrile diseases, rachitis, and, on account of its content of phosphorus, in neurasthenic conditions. Under its use not only is the condition of the blood improved, but an increase in the body weight and nourishment

is likely to take place. The author considers it an important addition to the preparations of iron already in use.—*Thérapeutische Monatshefte*, 1904, No. 3, p. 146.

The Physiological Action of Apocynum Cannabinum.—Dr. Horatio C. Wood, Jr., after an investigation of this drug, reports upon it thus: Its effects are very similar to those of digitalis. It slows the pulse and increases blood pressure, the latter effect being due to stimulation of the heart or of the vasomotor mechanism, or both. It stimulates the heart muscle directly, and, like digitalis, it causes a cessation of cardiac action through overstimulation. The author is inclined to believe that there is also an action upon the arterial walls. Studies show that the kidney circulation is diminished, due to a narrowing of the calibre of the vessels of the organ. The diuretic action of the drug is a consequence of the regulation of the circulation. The slowing of the pulse is caused by stimulation of the cardiac inhibitory centres. Like digitalis, apocynum is likely to disturb the stomach. It is possible that this effect is due to a different substance from that which causes the stimulation, and if the active principles were isolated we should have an exceedingly valuable drug.—*Therapeutic Review*, 1904, No. 3, p. 86.

The Therapeutics of Magnesium Peroxide.—MM. Gilbert and Jounier make the following report after a study of this agent. In doses of from 4 to 8 grains it relieves the symptoms of abnormal gastric fermentation (foul breath, regurgitation, nausea, gastric distention). In keratin-coated capsules containing from 3 to 4 grains it has proved valuable in diarrhœal conditions. Its good effect seems to be due to the liberation in the stomach or intestine of nascent oxygen.—*La presse médicale*, 1904, No. 25, p. 198.

Injections of Artificial Serum in the Vomiting of Pregnancy.—M. Condamin, on the ground that the vomiting of pregnancy is due to a general toxæmia, caused, perhaps, by the extra work put upon the various organs or by the retention of toxins in the blood, has attempted to relieve the condition by injecting artificial serum. He has proceeded thus: Food, both solid and liquid, is stopped for eight or ten days. Daily rectal injections of from three to four quarts of serum are given. If these are not tolerated by the bowel a few drops of laudanum are added to the injections or they are given under the skin. In eight or ten days fluid diet is allowed, and gradually the patient returns to ordinary food, the injections being continued meanwhile. This treatment has been employed in a number of cases with beneficial results.—*Journal de médecine de Paris*, 1904, No. 7, p. 64.

Sodium Salicylate in Gonorrhœal Epididymo-orchitis.—M. Carey reports 9 cases treated with this drug, which was administered in doses of 1 to 1½ drachms daily in solution. Only 1 patient complained of ringing in the ears, and this ceased upon diminution of the dose. The fear of evil effects upon the kidneys may be wholly disregarded. Unpleasant symptoms from the drug are likely to be rare, for the patients most subject to the inflammation in question are in the prime of life, when the emunctories are at their best. After a day or two of the treatment the symptoms are rapidly ameliorated. The pain disappears, and with it

the febrile movement and the insomnia. The tenderness is also quickly removed, the general condition is bettered, the testicle and cord return to normal size, and recovery takes place in about a week. Just as after-treatments by other methods, induration of the epididymis persists, but this seems to respond to the administration of potassium iodide. Treatment by the salicylate should not be employed as a substitute for local treatment, but in connection with it.—*Revue francaise de médecine et de chirurgie,* 1904, No. 12, p. 281.

Camphoric Acid as a Preventive of Catheter Fever.—D. A. FREUDENBURG recommends this substance in 15-grain doses, once, twice, or thrice daily, preferably in capsules, on account of its odor, commencing some days before the operation and continuing it afterward. Gastric disturbances contraindicate its use. It is believed to be a benefit in the treatment of cystitis as well.—*Gazetta degli ospedali e delle cliniche,* 1904, No. 38, p. 406.

The Treatment of Tuberculous Cystitis—M. HARTMANN recommends the following procedures in this condition: Into the empty bladder from 3 to 8 drachms, depending upon the tolerance of the organ, of iodoform 1 part, sterile liquid vaselin 20 parts are injected. The patient is instructed to watch the urine, and, upon the appearance of the oil, to stop the flow. Thus the pain caused by complete emptying of the bladder is avoided. Some individuals are able to retain the vaselin from three to six days. Reappearance of the pain shows that the vaselin has been wholly voided, and now instillations of 20 or 30 drops of iodoform 1 part, liquid guaiacol 5 parts, sterile vaselin 100 parts are given once or twice daily. At the same time capsules containing 0.15 grain of iodoform and 0.75 minim of creosote are administered. When surgical procedures, such as nephrectomy for unilateral tuberculous kidney or excision of a tuberculous ulcer of the bladder wall, are indicated they should be performed.—*Revue francaise de médecine et de chirurgie,* 1904, No. 13, p. 307.

Collargolum as a Prophylactic for Septic Processes.—DR. J. CAMERER advises prophylactic inunctions of unguentum Credé in all puerperal cases in which manual interference has been necessary or which seemed to have been rendered liable to sepsis by prolonged labor or repeated examinations. Thirty cases so treated recovered without complications. The procedure is particularly advisable in country practice, where aseptic principles are difficult to follow. The process consists in the inunction of 45 grains of the ointment twice a day for three days, using the legs and back alternately. At least thirty minutes are necessary for a proper inunction, and the rubbing should be continued until the black stain caused by the first application has entirely disappeared. —*Die Thèrapie der Gegenwart,* 1904, No. 2, p. 67.

Eucaine in Local Anæsthesia.—DR. H. C. WOOD thus describes the use of eucaine in infiltration anæsthesia. Powders containing 3 grains of beta-eucaine and 12 grains of pure sodium chloride are kept in stock. To make the solution for injection, one of these is dissolved in 3 ounces of boiling water. To this, when cool, 15 minims of 1 : 1000 adrenalin chloride are added. The whole of the solution may be used

for one infiltration if necessary, but usually less is sufficient. Even hernia operations may be done with this agent. It is necessary that a needle of platinum pointed with iridium be used, in order that it may be sterilized in flame immediately before use.—*Therapeutic Review*, 1904, No. 2, p. 52.

Potassium Permanganate in Viper Poisoning.—DOTT. ANTONIO MORI reports a successful instance, after a thorough discussion of the work done upon snake poisoning. A boy aged fourteen years was bitten upon the right hand by a viper. Ten hours afterward, while presenting to a marked degree the symptoms of poisoning, two injections of a 1 per cent. solution of potassium permanganate in the site of the wound; later intravenous injections at the elbow of the affected side were made. At four-hour intervals hypodermic injections of camphor were given, followed by as much coffee and milk as he could swallow. Recovery was complete on the ninth day.—*Gazetta degli ospedali e delle cliniche*, 1904, No. 28, p. 298.

GYNECOLOGY.

UNDER THE CHARGE OF

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ASSISTED BY

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Results of Alexander's Operation.—WALDSCHMIDT (*Zentralblatt für Gynäkologie*, 1904, No. 22) reports 185 cases from Kümmell's clinic, 101 of the patients being examined a year after the operation, with only one anatomical failure; 85 patients were entirely relieved from their former symptoms referable to the displacement; 9 women had passed through normal labors, and 10 were pregnant when examined. No case of hernia was noted. The writer insists on the limitation of the operation to cases in which the uterus is perfectly movable and the adnexa are healthy.

Hysterectomy for Obstinate Hemorrhage.—STOECKEL (*Zentralblatt für Gynäkologie*, 1904, No. 22) reports a case of endometritis in which curettement, followed by the injection of tincture of iodine and subsequently atmokausis (two minutes at 115° C.), were ineffectual. After prolonged hemorrhages the uterus was extirpated, when it was found that the diseased mucosa in both cornua had not been affected by the previous treatment.

Hysterectomy for Cancer of the Corpus Uteri.—BAEKER (*Zentralblatt für Gynäkologie*, 1904, No. 22) showed at the Hungarian Medical Association two uteri which he had extirpated for obstinate hemor-

rhage that had resisted repeated curetting. In one instance the patient had been curetted twenty times (!), the microscopic diagnosis being always "glandular endometritis," until the last examination pointed to probable adenocarcinoma. The writer believes that these cases illustrate forcibly the theory that endometritis is an important factor in the etiology of cancer. [Every gynecologist meets with similar cases in which the clinical symptoms point so strongly to the presence of malignant disease that he feels qualified in performing hysterectomy, in spite of the favorable prognosis of the pathologist.—H. C. C.]

Indications for Vaginal Section.—FOURNIER (*La Gynécologie*, April, 1904) limits posterior colpotomy to cases in which there is a distinct swelling in the cul-de-sac, associated with fever. He regards it as simply a palliative measure for the evacuation of pus, and that it should be understood in every case that the *cause* of the trouble has not been removed, so that a radical operation will probably be necessary later.

Indications for Splenectomy.—JORDAN (*Berliner klinische Wochenschrift*, 1903, No. 52) believes that with improved technique and statistics the indications for this operation have been unduly extended.

Rupture of the spleen is a positive indication for extirpation, over thirty successful cases having been reported. It may become necessary even in the case of a small wound, especially if infected.

Simple and echinococcus cysts justify splenectomy, eight cases of the former having been reported, with no mortality, and seventeen of the latter, with two deaths.

Four successful cases of extirpation of the organ for sarcoma, one for lymphosarcoma, and one for angioma are on record, but in all except one case of sarcoma there was a recurrence of the disease.

Leukæmia and pseudoleukæmia, in the author's opinion, are contraindications to operation, since every case thus treated has terminated fatally. Spleens enlarged from malaria and chronic hyperplasia can be successfully extirpated; also cases of hyperplasia in connection with cirrhosis of the liver (seventeen recorded operations, with three deaths).

Movable spleens, being usually diseased, should be removed. Splenopexy is to be considered. A rare indication for splenectomy is necrosis and perisplenitic abscesses, seven successful cases of which have been reported.

Lymphatic Infection in Cancer of the Uterus.—MME. ALTRAMARE (*Annales de Gynécologie et d'Obstétrique*, June, 1904), after a review of the writings of those who favor radical abdominal hysterectomy, principally on the ground that infected lymph nodes and periuterine tissues can be more thoroughly removed, concludes that logically the only real radical operation should include removal of the entire uterus, vagina, both broad ligaments, and ureters, and all the lymphatics as high as the iliac glands.

Statistics show that involvement of the lymph nodes occurs in only 20 per cent. of cases of cancer of the uterus, and that recurrences are nearly always local, occurring in the pelvic tissues, the bladder, or vaginal vault. The writer denies that the permanent results have been any better since the adoption of the radical operation. She concludes that

a systematic search for lymph nodes during an operation for extirpation of the cancerous uterus introduces an unnecessary complication and renders the prognosis less favorable, since the glands are often not found, and when removed the disease recurs in the broad ligaments the same as after vaginal hysterectomy. She believes that an improvement in the statistics of hysterectomy for cancer of the uterus is to be expected rather from early recognition of cancer, than from illusive attempts to remove all the outlying foci in more advanced disease.

Action of Caustics on the Endometrium.—RIELAENDER (*Zentralblatt für Gynäkologie*, 1904, No. 26) studied the action of 30 and 50 per cent. alcoholic formalin solutions, strong nitrate of silver, and tincture of iodine by introducing these drugs into the uterine cavity on an applicator twenty-four hours before extirpation of the uterus. The operation was performed for the relief of obstinate hemorrhages. The writer concludes that alcoholic solutions of caustics are preferable for intrauterine use, because they penetrate more deeply into the tissues. Applications are better than injections, as there is no risk of entering the tubes. Within twenty-four hours (!) after the application of a 30 per cent. alcoholic solution of formalin a slough was cast off and regeneration of the mucosa had begun.

[It is difficult to reconcile these conclusions with those of other competent observers who claim that several weeks elapse before regeneration of the endometrum is completed.—H. C. C.]

Deciduoma Malignum.—BAROZZI (*La Gynécologie*, June, 1904) contributes an article on this subject, with exhaustive bibliography, no new conclusions being reached. After an historical review, he discusses the pathological anatomy, stating that in the majority of the reported cases the mucous membrane is primarily involved, usually near the fundus, but the disease extends rapidly to the uterine muscle. The uterus is not enlarged until the later stages, and rarely reaches the size of the fetal head at term. Contrary to the conditions in cancer, in deciduoma metastases are so frequent as to form a distinctive feature of the disease; the lungs are their favorite seat, so that the pulmonary symptoms may be the most prominent. Metastatic nodules in the vagina are next in order of frequency, though any organ (and even the nervous system) may be involved. This tendency to metastasis is explained by the early destruction of the vessel walls by the plasmodial masses or syncytial cells, and their entrance into the blood.

Two varieties of deciduoma are recognized histologically, the typical characterized by the presence of ramifying plasmodial bodies, between which are nodules composed of mononucleated cells, and the atypical, in which small groups and isolated plasmodial bodies are seen. A mixed type has been described. It has not yet been determined positively whether one variety is more virulent than the other.

The onset of the disease may be so insidious that the results of metastasis may be apparent before the local condition is suspected. In most cases, however, the history of previous pregnancy and obstinate hemorrhages, with rapid decline in the general health, point to the probable diagnosis, which is confirmed by the removal of fragments of the neoplasm. Deciduoma usually attacks multiparæ between the ages of twenty and thirty years, the symptoms appearing between two

and four months after labor or abortion, though there are wide variations. The writer agrees with Durante in casting doubt upon cases in which from one to two years have elapsed since previous pregnancy, as an early abortion may have passed unnoticed, or the patient may have long had a placental polypus.

The prognosis is absolutely bad, for without operation the disease terminates fatally in from one to six months, though a few cases have been reported in which the patient survived for a year or more. The only known prophylaxis is to remove every bit of retained placental tissue after labor and abortion, and especially placental and hydatiform moles. If hemorrhages persist after thorough curettement, even though no neoplasm can be found, the writer believes that hysterectomy should be performed without delay. The surgeon should not be thrown off his guard by believing that the symptom is due to a "hemorrhagic endometritis." The only possibility of obtaining a cure lies in early operation, before metastases have occurred. Ladinski's statistics (124 operations, with 51 cures) are imperfect, since later writers have reported nine operations in which the patients were free from recurrence from one to six years afterward.

Recurrent Fibroma of the Uterus.—Groenzder (*Roussky Vratch; La Gynécologie*, June, 1904), while admitting that so-called "recurrent fibroma" is really sarcoma, contends that it is sarcoma of a peculiar type. He reports a case of persistent metrorrhagia and abdominal pain in a woman, aged forty-four years, from whom a necrotic intrauterine polypus was removed, presenting no microscopic evidence of malignancy. Ten months later a similar polypus was removed, metrorrhagia having returned six months after the former operation. The bleeding continued, and as hysterectomy was rejected, the operator was obliged to content himself with the excision of a third polypus, which differed histologically from the other two only in containing groups of suspicious ovoid cells. Finally, two years after the first operation, the patient re-entered the hospital with her uterus enlarged to the size of the fetal head at term. It was removed by laparotomy, and the patient was not seen for six months, when she returned with recurrence in the lumbar glands, and eventually succumbed.

On section of the uterus the endometrium was found to be replaced by soft granulation tissue. The uterine muscle around the tumor showed fatty degeneration and necrosis of the muscle fibres. The structure of the tumor presented somewhat the same appearance. The writer believes that the polypi first removed were sarcomata, their true character having been overlooked.

Follicular Carcinoma of the Ovary.—Voigt (*Archiv für Gynäkologie*, Band lxx., Heft 1), in describing a case of his own, concludes that it originated not in the primordial follicles, but in the superficial germinal epithelium by the ingrowth of follicular bodies, some of which formed pseudomucin cystomata and the other adenocarcinoma. He reviews Kossmann's theory that papillary as well as serous and simple adenocystomata of the ovary are developed from isolated masses of Müller's epithelium derived from the superficial layer. Just like the epithelium of Müller's ducts in the cervix, the same cells in the ovary may assume different characters.

OPHTHALMOLOGY.

UNDER THE CHARGE OF

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Ocular Complications of Bright's Disease —STRICKER, of Cincinnati (*Journal of the American Medical Association*, February 20, 1904), presents a study of these conditions, and reports 16 cases. All but 4 of these were cases of some form of neuritis or neuroretinitis; the 4 exceptions were: 1 venous thrombosis, 2 uræmic amaurosis, and 1 keratitis, in all probability a general uveitis. Of these cases 2 occurred during pregnancy as acute Bright's disease. Both are living, in 1 case with vision greatly impaired. Four were cases of chronic parenchymatous nephritis following acute diseases; all of these died. Ten were cases of chronic interstitial nephritis, 7 of which p oved fata'. He sums up in the following conclusions: 1. There are no ocular complications pathognomonic of Bright's disease. 2. The characteristic fundus picture—hemorrhages, areas of degeneration, white sp ashes in the macular region—may not be present; one may meet with any of the many manifestations of vascular or retinal inflammation due to toxins. 3. Ocular complications occur in only a mall percentage of Bright's disease, partly because lesions not causing functional disturbances are apt to be overlooked. 4. All the ocular complications are the result of a chronic uræmia. 5. The ocular lesions of Bright's disease are of most serious prognostic import as regards the life of the patient. 6. The prognosis is better in the acute form conditions, though the vision remains greatly impaired. 7. The amount of urea excreted in twenty-four hours is the best indication of the early or immediate fatal outcome of the case. 8. In pregnancy cases a low excretion of urea should call for immediate interference to save the eyesight, as well as the life of the mother. 9. In the choroidal and retinal changes the writer has found the amount of urea below the normal. He regards its retention or that of other excrementitious substances in the blood due to faulty kidney action as directly responsible for the inflammatory or degenerative changes.

Certain Cases of Asthenopia and Eye-strain which are Independent of Refractive Error and Muscular Imbalance.—DE SCHWEINITZ (*University of Pennsylvania Medical Bulletin*, June, 1904), after referring to the universally known ill-effects of anomalies of refraction, accommodation and motility of th eyes, comprising, indeed, fully 75 per cent. of ocular disorders, and whose influence is also felt in parts of the system remote from the eyes, observes that causes of eye-strain unrelated to the e anomalies have not unnatural y failed, perhaps, to receive the attention they deserve, although this side of the question has not been

entirely neglected. The writer proceeds to give a résumé of personal experience in this matter. These embrace: Simulation of eye-strain and asthenopia by symptoms depending upon the lithæmic state (the serious ocular disorders which may result from this condition, for example, various types of keratitis, iritis, etc., are not now under consideration). Some of the cases to which reference is made are as follows: Itching, burning, or formication of the eyelid margins. Œdema of the eyelids, tender spots in the ciliary body, wi h pinpoint ocular pain, foreign body sensations in the eye, subnormal amplitude of accommodation. For many of these conditions glasses are not a panacea. They are to be examined with the aid of the advanced physiological chemistry and treated in accordance with the results so obtained.

Glaucoma and Glaucoma Theories.—PATTERSON, Edinburgh (*Medical Press*, February 17, 1904), dealing first with the normal condition, pointed out that the aqueous humor was secreted by the epithelium in the ciliary region and eliminated by the filtration angle, and, to a less extent, by the vessels of the iris. The exact channels of outflow are determined by the elimination of Indian ink after injection into the vitreous. Leber's estimate that the fluid in the anterior chamber was renewed every forty minutes seems too high. There is no appearance of current in the anterior chamber, so that outflow must be very gradual. The intraocular pressure is intermediate between the arterial and venous capillaries, about 25 mm. Hg., subject to slight variations and not affected by accommodation. It can never, of course, exceed that of the arteries supplying the eyeball.

Turning to glaucoma, this was defined as a state of increased intraocular tension. Part of our lack of knowledge of pathology is due to the fact that attempts to produce it artificially in animals have met with little success. Another great obstacle is the fact that eyes were not enucleated at an early stage, but only when secondary changes had set in. The morbid appearances of such eyes are now perfectly well known, but it is impossible to say which of these changes is the primary cause of the disease.

A short discussion of the various theories of glaucoma follows. Von Graefe and Donders thought it was due to hypersecretion; Knies had ascribed it to a blocking of the filtration angle by adhesive inflammation of the tissues in that region; while Weber thought that a similar blockage took place in consequence of swelling of the ciliary body. While the lesion described by Knies was of the greatest importance, it could only be regarded as secondary, since it was absent in early cases of acute glaucoma. Priestley Smith's view, that, especially in hypermetropic eyes, the circumlental space becomes narrowed by the growth of the lens, which latter might be completely obliterated by swelling of the ciliary processes, pressing the root of the iris forward and occluding the filtration angle. There was, however, no direct evidence of this hypothesis. The theories of Panas, Abadie, and others were passed in review and shown to be untenable or inadequate. Stress was laid on the frequency with which chronic glaucoma was associated with general vascular changes, and while some forms of eye (hyperopic) were predisposed to glaucoma, others (myopic) were not. Careful examination of the circulatory system by modern instruments for investigating blood pressure might throw some light on the pathology of the subject. Little more

was to be gained by examination of old glaucomatous eyes or experiments on animals, but if, as he was informed, that it was true that domestic pets kept under highly artificial conditions—*e. g.*, pampered lap-dogs—were occasionally the subjects of glaucoma, it might at some time be possible to get an eye in the early stage from this source.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

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Chronic Coryza.—Dr. L. Jacquet, of Paris, contributes a communication (*Annales des Maladies de l'Oreille, du Larynx*, etc., March, 1904) concerning an albuminuric patient in whom an attack of severe and obstinate coryza was relieved during treatment of the albuminuria by omitting salt from the diet. On experimentation he found personally that by diminishing the salt in his own food he could quiet a coryzaic condition to which he is subject. He, therefore, suggests that this treatment be essayed for ordinary chronic coryza.

Hay Fever.—In a paper on "The Relation of the Chemistry of the Saliva and Nasal Secretions to Diseases of the Mucous Membrane of the Mouth and Upper Respiratory Tract, with Special Reference to Hay Fever," and read before the Section on Laryngology at the recent meeting of the American Medical Association (*American Medicine*, June 18, 1904), Dr. D. Braden Kyle, of Philadelphia, expressed his belief in the importance of the consideration of the individual character of these secretions which, under certain conditions, are irritating, while non-irritating in others. He advises treatment directed toward rectifying the pathologic conditions of the secretions to be begun several weeks before the usual time for the hay fever attack to come on in individuals who have been chronically susceptible. In acute attacks the same line of treatment is to be carried out, though more vigorously, the secretions being rapidly shifted from acid to alkaline, or *vice versa*. Dr. Kyle reports 80 per cent. to 90 per cent. of cures in patients treated on this basis.

Reflex Apnœa and Cardiac Inhibition in Operations upon the Respiratory Tract—In a paper on this subject read at the recent meeting of the American Medical Association by Drs. William Harmar Good and W. G. B. Harland, of Philadelphia (*American Medicine*, June 11, 1904), and based especially on observations during adenoid operations and during intubation in which cases of instant death are on record, they conclude that the origin of reflex apnœa and cardiac inhibition is through the medulla by irritation of trifacial and sensory

branches of the vagus; that inhibition may be caused by irritation of the mucosa of the nose, rhinopharynx, larynx, and lungs; that obstruction to respiration is indicated by cyanosis and full pulse, while reflex inhibition produces pallor and slow, weak pulse.

Infections of the Lymph Glands of the Mouth and Throat—Dr. Robert T. Morris, of New York, read a paper on this subject before the First District Society of the State of New York last December (*The Dental Cosmos*, June, 1904). He calls attention to Ludwig's angina and other affections proceeding from infections in the mouth. He discusses the methods of treatment that should be instituted from this point of view.

Melanotic Sarcoma of the Soft Palate.—At a recent meeting of the Laryngological Society of London (*Journal of Laryngology, Rhinology, and Otology*, June, 1904), Dr. J. B. Ball showed a case of melanotic sarcoma of the soft palate in a man, aged fifty-three years. The patient had first noticed some black patches on the palate two years previously. Some seven or eight months ago a growth commenced on the soft palate, but as it gave no inconvenience little notice of it was taken until three weeks ago, when it bled, and he then showed it to his doctor. A dark-looking, flattened, somewhat mushroom-like growth covered an area about the size of a shilling on the middle of the soft palate. There were numerous black patches on the hard and soft palate and on the upper gums. There was some slight glandular enlargement under the chin near the middle line. The patient had lost about a stone in weight during the last twelve months.

Pachydermia Laryngis.—In discussing a laryngoscopic image of a woman, aged forty-three years, shown to the Laryngological Society of London by Mr. de Santi (*Journal of Laryngology, Rhinology, and Otology*, June, 1904), the President, Dr. McBride, called attention to the fact that the pachydermia involved the anterior commissure as well as the interarytenoid space and vocal processes to which this lesion is confined in most instances.

Treatment of Ulcerated Epitheliomas of the Upper Air-passages by Applications of Adrenalin.—Dr. Georges Mahu reports (*Annales des Maladies de l'Oreille, du Larynx*, etc., March, 1904) a number of instances of epitheliomas of the tongue, pharynx, larynx, and other regions very much benefited by applications of adrenalin, 1:1000. Hemorrhages seemed very easily arrested, and the patients improved very much for the time being. Attempts to hasten matters by injections of the solution were injurious, and led to the development of new vegetations.

Removal of Pin from the Lung through the Natural Passages.—Dr. E. Fletcher Ingals reports (*Journal of the American Medical Association*, April 30, 1904) a case in which, with the aid of a Killian bronchoscope and tube forceps, he was able to remove from one of the divisions of the right bronchus, where it had been detected by radiography the day previous, a large glass-headed pin which had been inhaled into the windpipe of a young woman nearly a year before.

DERMATOLOGY.

UNDER THE CHARGE OF

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The Tuberculous Nature of Angiokeratoma.—PAUTRIER (*Archiv für Dermatologie und Syphilis*, Band lxix., Heft 1 and 2) believes that angiokeratoma should be placed among the tuberculous affections of the skin, and presents a number of histological facts in support of this view of its etiology. The occurrence of this affection in those who present certain and well-marked evidence of tuberculous disease and its association with other tuberculous eruptions are adduced as clinical evidence of the great probability of its tuberculous character. After referring to a number of cases reported by other observers in which angiokeratoma was associated with other well-defined tuberculous affections, he reports the case of a young woman under his own observation, in whom angiokeratoma coexisted with typical lupus pernio and tuberculosis of the lungs. The father of the patient had a typical lupus erythematosus of the ears, and a maternal uncle and an aunt had died of tuberculosis of the lungs.

The histological changes correspond to those found in the tuberculides, more especially to the necrotic tuberculides.

A Hyperkeratosic Exanthem in Severe Gonorrhœal Infection.—BAERMANN (*Archiv für Dermatologie und Syphilis*, Band lxix., Heft 3) reports in detail 2 cases of a rare eruption associated with severe general gonorrhœal infection. The eruption was a polymorphous one and occurred under two forms: 1. Disseminated lesions distributed over the whole body. 2. Aggregated lesions upon the hands and feet, more especially the fingers and toes. In the disseminated variety scaly lesions seated upon a non-inflammatory base were scattered over the entire body, more particularly the extremities, rarely upon the scalp, and almost never upon the face. The eruption was composed of scales much like the thick scales seen in psoriasis complicated with a local seborrhœa; it was infrequently preceded by a vesicular stage. Very often, especially in the older and larger lesions, the scales were lamellated like the shell of an oyster, and occasionally they formed cone-like structures. The color was a dirty-yellow, the lesions showed a certain translucency, and they sometimes looked as if varnished. The scales were strongly adherent, and when forcibly removed, showed a dry or moist, red, papillomatous base. The form localized upon the hands and feet was much more common than the disseminated form, and presented quite a different picture. Occasionally a few small lesions like those already described were found upon the hands and feet surrounded by a callus-like thickening. More commonly the horny layer of the

palms and soles was thickened diffusely, was of a dirty, yellowish-brown color, and was marked, more especially on the borders, by deep furrows. Upon such a base were situated discrete or confluent, moderately smooth or deeply fissured, cone-like prominences. Points of pressure upon the palms and soles were especially affected, as well as the nails and the nail-folds, particularly of the toes, the nails becoming opaque and brittle. The nails in some instances were lost completely, the nail-bed being covered only with a thin, oozing layer of epidermis. Oftentimes these lesions occurred in plaques upon the lower extremities, especially on surfaces exposed to friction or in contact. Those extremities were most affected in which, owing to disease of the joints, a considerable degree of muscular atrophy had taken place. The microscopic changes consisted of a moderate dilatation of the cutaneous vessels, which were surrounded by an abundant infiltration of leukocytes. In the deeper layers of the epithelium were numerous migratory cells, and the papillæ showed proliferation. The horny deposits consisted of incompletely cornified, parakeratotic cells with still demonstrable nuclei. Foci of softening were present in the horny cones and in the thicker scales. Gonococci were never found in the eruption.

Pityriasis Rosea.—Harvey P. Towle (*Journal of Cutaneous Diseases*, April, 1904) considers this disease in the light of reported cases and his own experience, and concludes, from an analysis of a series of 202 cases, that the disease occurs in two forms, the macular and the circinate, with about equal frequency. It occurs most often on the trunk and the upper parts of the extremities, but occasionally is confined to one part. It is most common in the autumn, and is met with more often in women than in men. It may occur at any age, although most frequent between twenty and thirty years. As a rule, there are no prodromata or accompanying disturbance of the general health. Itching may or may not be present. Histologically, the chief changes are in the cutis.

Acne Rosacea and Its Treatment.—A. D. Mewborn (*Journal of Cutaneous Diseases*, April, 1904, p. 192) calls attention to the value of the so-called scaling treatment by such remedies as a solution of resorcin, 10; sulphur, 10, and tincture of soft soap, 40, used for three successive nights during each week. A case is given in which the use of the high-frequency current and the Roentgen ray alone, used for several months, had failed, but was cured by opening the pustules with a lancet and using the scaling treatment referred to. He thinks the Roentgen rays should not be employed until the milder forms of treatment have failed.

Treatment of Ringworm with Chrysarobin.—Hodara (*Jour. des mal. Cut. et Syph.*, August, 1903) recommends a solution of equal parts of glycerin and chloroform containing from 5 to 10 per cent. of chrysarobin, to be applied daily after shaving of the scalp, continued until œdema and slight erythema are produced. Four or five months are required to effect a cure.

Pityriasis Rubra (Hebra).—Tschlenow (*Arch. für Derm. und Syph.*, Band lxiv. Heft 1) considers the following as the more important pathognomonic symptoms of this rare disease. Loosening of the corneous layer

in the form of small lamella and the presence of nucleated cells, more or less disappearance of the corneous layer, thickening of the mucous layer, followed by thinning of the same, disappearance of pigment in the basal stratum, augmentation of the connective tissue, bloodvessel changes, and atrophy of the skin. He distinguishes clearly between this disease and dermatitis exfoliativa. He deplores as unscientific Brocq's group of pityriasis rubra and Besnier's erythrodermies exfoliantes.

The Action of Formalin upon the Fungus of Favus.—BOGROW and SCHARKEWITSCH-SCHARSCHINSKY (*Dermatologische Zeitschrift*, Band xi., Heft 5), as the result of experimental investigations with formalin in favus, conclude as follows: The 5 per cent. watery solution of formalin kills the *achorion*, cultivated from epilated hairs after the method of Plaut, in twenty minutes, and may act still more rapidly. An increase in mechanical hindrances, such as particles of the nutrient media clinging to the culture or thickness of the mycelium, may completely annul the action of watery solutions. Those parts of the hair which are in the skin are inaccessible to solutions of formalin in water, probably on account of the fat in the hair. The employment of formalin solutions does not facilitate the treatment of favus. As to the effect of spirituous solutions and formalin vapor upon the *achorion*, further observations are desirable.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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Ankylostomiasis (Uncinariasis) not Essentially a Miners' Disease.—But a few years ago ankylostomiasis was regarded as a parasitic disease peculiar to certain localities and associated especially with coal-mining and other occupations carried on underground, and the vehicle of infection was thought to be polluted water. In 1902 DR. CHARLES WARDELL STILES (*Public Health Reports*, October 24, 1902) discovered that in some parts of the South it is the most common disease of man, and that the infection is less severe and less common in the mining districts than on the farms and plantations of the sand district. HARRIS (*American Medicine*, November 15, 1902) and other Southern observers confirmed the conclusions of Stiles, by whom, also, it was pointed out that the dissemination of the parasite is not due to polluted water, but to polluted soil; and BAKER (*British Medical Journal*, March 28, 1903) asserted that the embryos cannot live in water. Now, the disease has been found to exist in many districts of Europe where it never before was suspected, and it would appear that it is very widely disseminated and has been for a long time. With regard to its being in Europe essentially a miners' disease, the observations of the DRS. IBERER (*Münchener*

medicinische Wochenschrift, 1903, No. 23, p. 992) are of interest, since they are in full accord with the findings of American investigators. They are of the opinion that sunlight not only is not harmful, but distinctly favorable to the development of the larvæ. On the other hand, water at 44° F. to 61° F. kills the eggs, embryos, and larvæ. They have had occasion to examine large numbers of peasant lads who have never worked in the mines and yet have yielded, in very many instances, large numbers of the parasites. Hence they conclude that the disease is endemic on the farms. Even when the parasites were found in great numbers the subjects were often neither poor in blood nor otherwise ailing. Many of the lads who went away for their three years' military duty returned, at the expiration of their terms of service, still infested, but with no history of having suffered in any way in consequence. Of the miners examined, no less than 94 per cent. were found to be infested, but not more than one in four was ever incapacitated, even temporarily.

Meat Poisoning and Paratyphoid.—An outbreak of meat poisoning in Düsseldorf, in which fifty-seven persons fell sick during a period of six days after eating chopped horsemeat, has led to interesting investigations concerning the bacteria that have been demonstrated as the exciting causes of this and other outbreaks of the past. In this outbreak one of the victims ate the meat in the form of boiled sausage, three ate it stewed, and the rest ate it raw. The meat was unobjectionable as to taste, odor, and appearance; it was derived from different animals, but was all from one shop. It is an interesting fact that the butcher who minced and sold the meat bought part of it, a hindquarter, of another butcher, who sold the other three quarters to customers not one of whom was made sick. In the great majority of those who were attacked, the symptoms were vomiting, diarrhœa, and vertigo; thirty-one were sick enough to need a physician, not a few were incapacitated for a long time, and one, a boy of nine years, died. From the spleen of this victim a short bacillus was isolated that proved to be very virulent for mice and guinea-pigs, less so for rats and rabbits, and not at all for dogs and cats. Boiled cultures were not pathogenic for guinea-pigs and rats, but were for mice. This organism has been studied carefully by Dr. H. Trautmann (*Zeitschrift für Hygiene und Infectionskrankheiten*, xlv., p. 139) and compared with *B. friedebergensis* (Gaffky and Paak), *B. enteritidis* (Gärtner), *B. breslaviensis* (Kaensche), *B. morsulensis* (van Ermengern), and the bacteria of other outbreaks of meat poisoning investigated by Fischer, Abel, Günther and others; also with Basenau's *B. bovis morbificans*, Brion-Kayser's paratyphoid bacillus of type A. and Schottmüller's, Hünerman's, and Conradi, Drigalski and Jürgens' paratyphoid bacilli of type B. He comes to the conclusion that these organisms, while presenting slight differences in form, size, staining properties, motility, and growth on culture media, show no fundamental difference and are merely variations of one and the same organism. In a second communication (*Ibid.*, xlvi., p. 68) he cites certain variations in the kind and severity of symptoms and in the order of their appearance are dependent upon these slight variations in the bacterial races and upon the degree of virulence and individual susceptibility. In meat poisoning the initial disease is an animal disease, and when the animal is killed on account of sickness and the meat is sold as food for man, containing the pathogenic organisms and their poisonous products, it may cause after some hours, or more commonly some

days, a train of symptoms of varying severity. It may result in violent gastroenteric symptoms with consequent expulsion of the offending material, or absorption of the poison may occur and produce general systemic disturbance, the severity of which varies according to dose and individual peculiarity. In the lesser cases we may observe, in addition to vomiting and diarrhœa, abdominal pain, headache, backache, dizziness, general malaise, skin eruptions, and the like; in the more severe cases, unconsciousness, delirium, and the choleraic condition. Many cases of meat poisoning can hardly be distinguished from paratyphoid, and severe cases are sometimes difficult to distinguish from real typhoid. Indeed, many outbreaks of meat poisoning have been diagnosed incorrectly as typhoid. Trautmann believes that the typical meat poisoning is a most acute, and the paratyphoid condition is more a subacute, manifestation of an etiologically similar disturbance. Since the urine and feces of the sick animals and of paratyphoid subjects can reach water supplies equally well with typhoid excreta, the mode of infection and spread may be similar.

Investigation of the Düsseldorf outbreak showed among other things the following interesting facts: The premises of the butcher who sold the meat, and his tools, including the hashing machine, were in a condition of great uncleanliness. The hindquarter which he obtained elsewhere made people ill, although the rest of the careass caused no trouble; this hindquarter was not mixed with other meat, and it was probably infected by the dirty implements.

Fleas and Plague.—Discussing a criticism of a report of an outbreak of plague that in respect to transmission by fleas "the weakest link in the chain is in reality the absence of any proof that the rat flea is under any circumstances so commonly parasitic to human beings as to become an etiological factor of any epidemiological significance whatever," Dr. J. S. C. Elkington, of Hobart, Tasmania (*Public Health*, July, 1904, p. 645), points out that the very marked differences in structure and habits shown by the different species and genera of fleas that infest rats make it as unscientific to speak of the rat flea without qualification in connection with plague as to speak of the mosquito in general as the conveyor of malaria. In Bombay and in certain parts of Australia, the most common rat flea is a pulex that closely resembles that which infests man, while in England it is one of another genus (Ceratophyllus) and differs widely from the two above mentioned. The rat flea of New South Wales, Victoria, and West Australia resembles closely the *Pulex pallidus* of Bombay, but the common rat flea of Tasmania and New Zealand differs widely from either, as does that of England. The rat flea (pulex) of Bombay and Victoria will under certain conditions feed vigorously on man, but the Ceratophyllus and Typhlopsilla genera can be induced to do so only with great difficulty, if at all, and to this fact may be due Galli-Valerio's negative results. The flea that infests man may be starved into feeding also on rats. Having in mind the following facts, it appears that the flea cannot be dismissed offhand as an innocent agent in connection with plague: 1. Fleas of certain species may carry virulent plague bacilli several days, and the bacilli can multiply without harming the insect. 2. The common rat flea of certain localities wherein rat plague is associated habitually with human plague is a pulex closely resembling the *Pulex irritans* of man, while that of certain other localities wherein rat plague is not so associated

belongs to another genus or other genera, differing widely in structure and apparently also in habits. 3. The inoculation of blood containing plague bacilli or of the bacilli separated from the blood of either rat or man will produce plague in man. 4. The rat pulices of Bombay and of certain parts of Australia, at least, will feed on man when hungry, and the *Pulex irritans* will similarly feed on rats. 5. The plague bacillus probably exists in the blood of every fatal human case at some time and certainly does so in great numbers in the septicæmic form of the disease. It also exists in great numbers, as a rule, in the blood of plague-stricken rats.

The Possibility of Tubercular Infection through Books from Public and Circulating Libraries.—The report that a number of clerks in a public office in this country had become tuberculous through handling books that had been infected by another who had had the habit of wetting his fingers with saliva when turning the leaves suggested to Dr. I. Mitulescu (*Zeitschrift für Hygiene und Infectionskrankheiten*, xliv., p. 397) an examination of popular library books, which, passing from hand to hand, must become exposed to infection from tuberculous readers. Thirty-seven books and periodicals, chiefly novels and stories, from three to six years old and all very dirty, especially on the edges and corners, constituted the first lot examined. The results of animal experimentation conducted on the usual lines demonstrated the presence of virulent tubercle bacilli in more than a third of the books; but the development of the disease was very slow and the amount of general infection was small, which facts suggest only moderate virulence and limited numbers of bacilli. A second lot of 60 books, including 20 that had been two years in use, 20 one year, and 20 six months failed to yield any tubercle bacilli. Of the 120 guinea-pigs employed, 31 died of various acute infections, but the remaining 89 after being kept from three and a half to four months were killed and examined, but showed no evidence of tubercular infection. The books of the first lot that gave positive results were old and dirty; the leaves of some of them stuck together. The other books were comparatively clean, having been much less long in service. The difference in infectivity (for both lots had doubtless been handled by consumptives) probably resides in the fact that tubercle bacilli will live longer in the moist dirt of old books than on the fresh, clean surface of new ones, on which the sputum is more easily and completely dried. It is not to be assumed, however, that comparatively new books may not convey infection, for they may be read by many and pass quickly from one to another; but the danger is greater with old books well encrusted with the protective dirt. The public should be taught not to wet the leaves of books while reading, and one should always wash the hands carefully after contact with books whose history is not known.

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THE

AMERICAN JOURNAL OF THE MEDICAL SCIENCES.

NOVEMBER, 1904.

A CASE OF DISLOCATION OF THE ATLAS,

SHOWN BY A SKIAGRAM, CAUSING PARALYSIS OF THE LEFT ARM AND THE SYRINGOMYELIC DISSOCIATION SYMPTOM ON THE OPPOSITE SIDE.

By James Hendrie Lloyd, A.M., M.D.,
of Philadelphia.

Some years ago I put on record two cases of trauma of the cervical region of the spinal cord simulating syringomyelia.[1] These cases were illustrated with photographs, and eventually post-mortem findings were reported in both of them. By a coincidence each of these patients had sustained two severe accidents quite dissimilar in type, and these accidents had resulted in fracture and dislocation of some of the cervical vertebræ, with marked deformity of the neck. Both cases had been of a goodly number of years' duration.

The fact of special interest in those two cases was the close similarity which they presented to the now well-known and classical picture of syringomyelia. Syringomyelia was not quite so well known ten years ago as it is now; and in fact, although here in Philadelphia we had been fairly prompt in recognizing and recording some cases of it, the disease was still rare enough to be interesting. A case of my own in 1893 was one of the first published in America with full microscopic findings. My recollection is that the disease was not much talked of nor widely recognized in this country before

[1] Traumatic Affections of the Cervical Region of the Spinal Cord Simulating Syringomyelia, Journal of Nervous and Mental Disease, June, 1894, p. 345. A Study of the Lesions in a Case of Trauma of the Cervical Region of the Spinal Cord Simulating Syringomyelia, Brain, 1898, xxi. p. 21. A Study of the Lesions in a Second Case of Trauma of the Cervical Region of the Spinal Cord Simulating Syringomyelia, Journal of Nervous and Mental Disease, February, 1900, p. 65.

1892 and 1893, although it was known in a general way from the reports of a few European observers, especially Leyden, but regarded rather as a pathological curiosity. Gowers' first edition, published in 1886, contains a fairly good anatomical description, but a very inadequate clinical account. In Bruhl's monograph on syringomyelia, printed in 1890, there is a noteworthy scarcity of American names in the extensive bibliography, not because of French indifference to American work, but because very little American work in this field had been done. Van Gieson, of New York, had published some autopsical findings in 1889, and he was probably the first American in the field with a microscope. Mere clinical reports of a few cases that may have been syringomyelia had been made by a few American observers, but they had not been confirmed, by autopsy.

I mention these few facts merely to show how little had been seen at that time of what I may call the syringomyelic syndrome; certainly it was a rare thing, if not unprecedented, to find this syndrome in two cases, both of them due to trauma, and neither of them presenting a cavity formation in the cord.

But a further and special point of interest in those two cases was in the fact that they both presented lesions which were partially unilateral, that is, of a unilateral type, and this fact led to some interesting conclusions on the subject of sensory conduction in the spinal cord.

The observations, briefly stated, were as follows: The dissociation symptom, or rather the thermoanæsthesia and analgesia, were present on the side *opposite* the main lesion, while tactile anæsthesia, with involvement of the motor tracts, was present *on the side* of the lesion. This was so in both those cases. I discussed at length, in my reports of those two cases, the grounds for supposing that these symptoms indicated that the fibres for the heat and cold senses and for pain, passing in by the posterior roots, decussate in the gray matter and pass upward in the anterolateral tracts of the opposite side, while the fibres for simple touch pass up in the posterior columns without decussating. This seems to be the obvious explanation of the symptoms. It suggests also that our conception of the Brown-Séquard syndrome will have to be modified to the extent of recognizing that tactile anæsthesia and thermoanæsthesia and analgesia are not of necessity present on the one side, but on opposite sides. These reasons in detail it is hardly necessary to repeat here; they can be read in the original papers.

The case which I have to put on record in this paper presents some points of marked resemblance to the other two, and also one or two features that seem to be quite unique. The man has been under my care in the Methodist Hospital for several months, and, as in the other cases, he has suffered from not only one but two

very severe and successive injuries. I am indebted to Dr. Imboden, the resident physician, for clinical notes.

J. W., aged twenty-one years, admitted January 12, 1904. Born in Philadelphia and has resided here during entire life. Uses tobacco in moderation, but alcohol to excess.

Previous Medical History. So far as he knows he never had any of the usual diseases of childhood except pertussis.

Previous Surgical History. When thirteen years of age he bruised the left leg below the knee while riding a bicycle, and this accident required the removal of some necrotic bone in this region. On the 16th of September, 1903, he had been drinking quite heavily in the morning, and while driving on a cart he fell off during an attempt to check the horse, which had become somewhat unmanageable. He struck on his left shoulder, the cart-wheel passing over the back of his neck. He was unconscious for an indeterminate period, being brought into the surgical dispensary of the Methodist Hospital, and a fracture of the jaw was diagnosed, but no spinal injury was recognized. He was sent to the surgical ward and remained there twelve days, and after his discharge he continued to come to the dispensary and was treated for an abscess of the jaw, presumably a result of infection through the mouth incident to or as a result of the fracture of the jaw. During all this time he was unable to turn the head without at the same time rotating the shoulders, and there can be little doubt that his spine had been injured in this first accident.

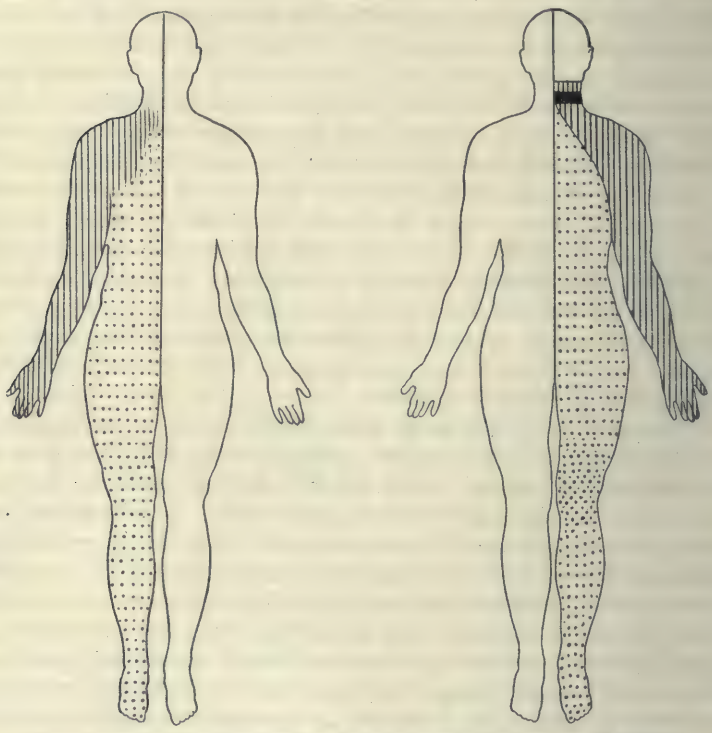
On January 12, 1904, about four months after the first accident, while the man was walking on a slippery sidewalk, both feet slid from under him and he fell on the left shoulder, striking the back of his head on the sidewalk with great force. This rendered him unconscious for about five minutes, and when he regained consciousness he was unable to move any of his limbs. This inability (motor) lasted for about half an hour, after which he slowly gained power, first in the legs and then in the right arm, but none returned in the left arm. As the man was unable to stand, the patrol was sent for and he was brought to the dispensary, where it was found that when he attempted to stand he would totter and fall if some one did not catch him. The patient stated that when he was trying to stand his back felt like a piece of paper, and it seemed to him that his spine was "*wabbling about.*" A rough test showed tactile sensation to be intact in all limbs, but practically no motor ability in the left arm. After remaining in the surgical ward for a short period, the patient was transferred to my care in the medical ward. His condition was as follows:

The patient had a marked deformity in the neck. The head was twisted to one side and slightly rotated, and the deformity was most prominent on the left side. With a finger in the pharynx the deformity could also be felt as a projecting mass on the posterior wall

of that cavity. The head was held in a very rigid and unnatural position, but there was no complaint of pain.

Motor Symptoms. The patient was paralyzed in the left upper extremity. He could not move the left arm at all, but he could flex and extend the forearm at the elbow. He could neither pronate nor supinate the forearm. He could flex and extend the thumb and index finger, but could not flex the middle, ring, or little finger; neither could he separate the fingers. The electric reaction in the affected muscles was not significant except in the deltoid and

FIG. 1.



Thermoanæsthesia and analgesia on the side opposite the paralysis of motion.

pectoralis, in which the faradic contractility was slightly diminished. There was no atrophy of the muscles, nor fibrillation. There was no paralysis in the left leg, a fact which is important, nor in the right arm or leg. There was no paralysis of the bladder or rectum. There was no involvement of the spinal accessory nerve, nor of the phrenic nerve, nor of any muscles of respiration. In fact, pressure symptoms were remarkable for their absence.

Sensory Symptoms. There was very marked loss of thermic sense in the *right* arm and forearm (that is, on the side opposite the motor

paralysis). The thermic sense was confused in the remaining parts of the right side, extending from the region of the fourth cervical vertebra. There was also analgesia of the entire *right* side from the region of the fourth cervical vertebra, also more pronounced in the arm and forearm.

Above the fourth cervical vertebra was an area one inch wide, which was hyperæsthetic; above this zone sensation shaded rapidly to normal.

There was no tactile anæsthesia anywhere, either on the left or right side. All these tests were made with great care, and sugges-

FIG. 2

Anæsthesia in the area of the great occipital nerve.

FIG. 3.

Case of dislocation of the atlas.

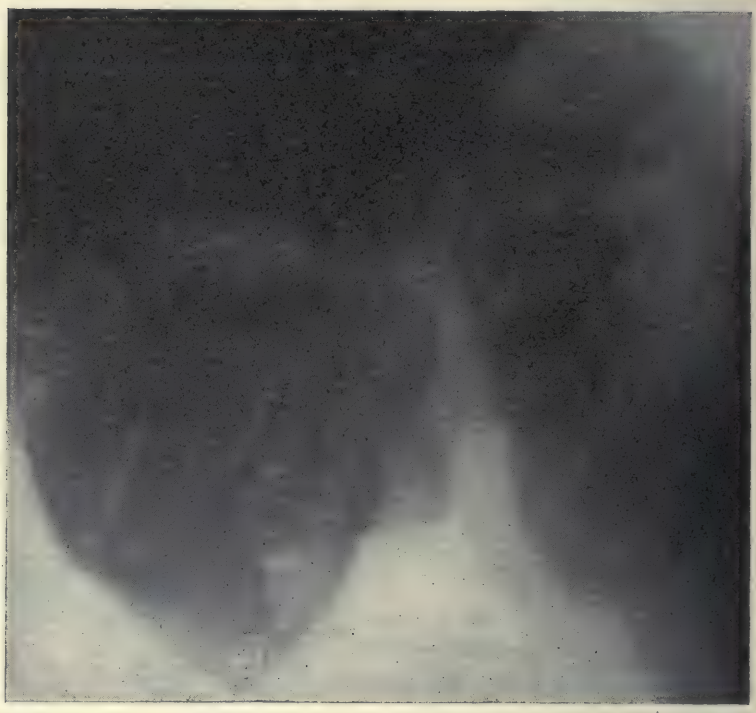
tion was avoided as much as possible. The patient never exhibited any of the stigmata of hysteria, and these sensory disturbances were not transferable. There remains, however, to note one sensory disturbance which may possibly be of great significance. This was a distinct area of tactile anæsthesia in the region of the distribution of the great occipital nerve of the left side. The great occipital nerve comes off from the second cervical nerve, and this second cervical nerve emerges from the spinal canal between the atlas and the axis. The involvement of this nerve, in view of what is shown by the skiagram, is significant, and is possibly the most important localizing symptom in the case.

The patient's sensory symptoms improved during his stay in the hospital, and eventually almost disappeared, but the motor paralysis in the left arm and forearm has persisted, and the deformity in the cervical region is unchanged.

The interpretation of the symptoms in this case has not seemed to me altogether easy.

The skiagram, which I exhibit, shows that the lesion is very high, and in fact the atlas appears to be displaced. The vertebræ below it, beginning with the axis, are in place, as is shown quite

FIG. 4.



Skiagram of dislocation of the atlas.

clearly by the relative positions of their spinous processes and by the distinctness of the intervertebral spaces. I have therefore taken the liberty of calling it a case of dislocation of the atlas, although I am fully aware that this is usually considered to be promptly fatal. Certainly it is difficult to conceive how the atlas can be dislocated and immediate pressure not occur on vital regions of the cord. But I call particular attention to the fact that displaced vertebræ can be felt in the pharynx, although by mere digital examination it is of course not possible to say what vertebra or vertebræ this may be. But

it must necessarily be high in the neck, for only the first four, possibly five, cervical vertebræ can be reached by a finger in the pharynx. A symptom of especial localizing value is the anæsthesia in the distribution of the great occipital nerve. This clearly indicates a high lesion, for the great occipital nerves are branches of the second pair of cervical nerves, and these pass out between the atlas and the axis.

The motor paralysis of the left arm alone is extremely difficult to account for. The brachial plexus passes off far below the apparent level of the lesion, and the fact that the leg is not involved shows

FIG. 5.

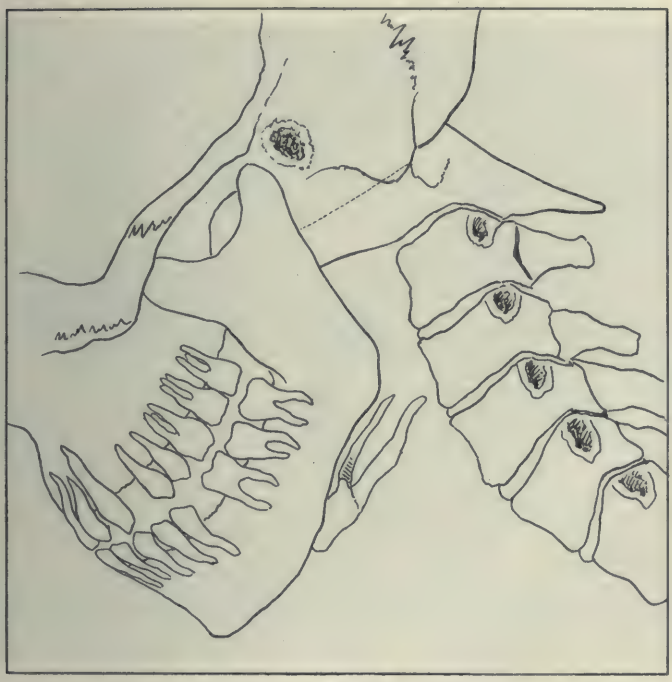


Diagram showing the tilting forward of the head in front of and slightly off of the vertebral column. The drawing is necessarily diagrammatic in the region of the atlas, as the details do not appear clearly in the skiagram.

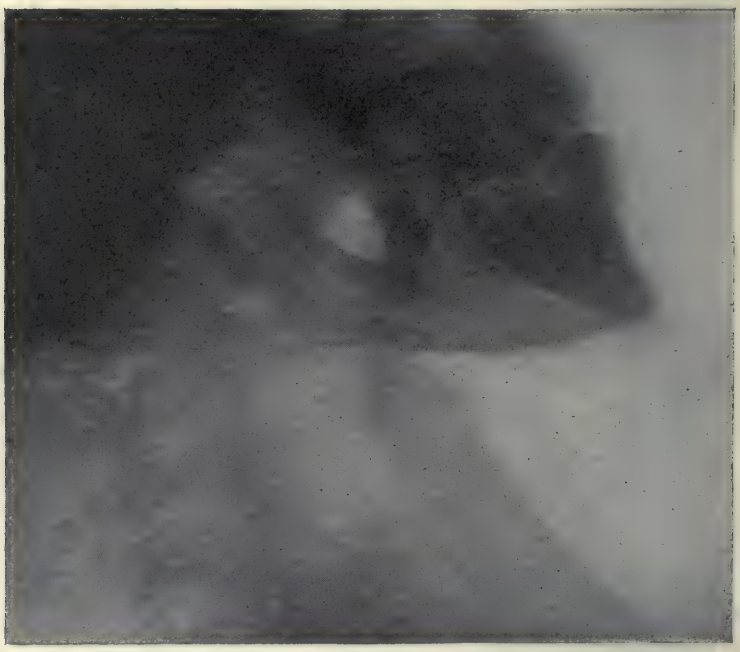
that the arm paralysis is not due to pressure on the lateral tract. Again, the arm paralysis is of the peripheral type, as would be due to a lesion of the anterior nerve roots, for there is some muscular atrophy with faradic changes.

The sensory symptoms seem to indicate a very localized pressure on the anterolateral region; that the posterior columns are not involved is shown by the absence of tactile anæsthesia.

Dr. Walton, of Boston, has recently reported several cases of dislocation of the cervical vertebræ, and has very clearly pointed out their mechanism. A displacement of the articular surfaces of

two adjoining vertebræ, with only a slight forward dislocation of the bone on one side, can cause such a deformity as this patient has without much if any pressure on the cord. Such dislocations have been successfully reduced, and have even reduced themselves spontaneously during sleep or during ether anæsthesia. But in case of the atlas we have to reckon with the odontoid process of the axis. The query arises, Could this odontoid process be fractured and allow the atlas to slip? Finally, Can there be two lesions, one of the atlas and one lower in the spine involving the anterior roots, that go to

Fig. 6.



Skiagram of normal skull and spinal column.

form the brachial plexus? The fact that a dislocation of the atlas may occur, and the patient continue to live for weeks and even years, is proven by several well-authenticated cases. The following references are to some of these cases.

Handyside[1] described a case of *spontaneous* dislocation of the *processus dentatus*, with ankylosis of the upper part of the spine, and unattended with any symptom of paralysis. This case came on during a severe attack of rheumatic fever, and its causation was obscure. There was no caries. This man lived ten years and

[1] Edinburgh Medical Journal, 1840, vol. liii. p. 876.

worked at his forge. He died very suddenly with asphyxia. At the autopsy the right inferior articular surface of the atlas was found dislocated downward and forward over the corresponding articular surface of the axis, and ankylosed. There was also ankylosis of the occipital bone to the atlas. The spinal canal was reduced to a space measuring two lines in some diameters, and the lower part of the medulla oblongata was compressed.

Stanley[1] reported a case of long-standing ankylosis of the five superior cervical vertebræ, with dislocation of the atlas. The clinical

FIG. 7.

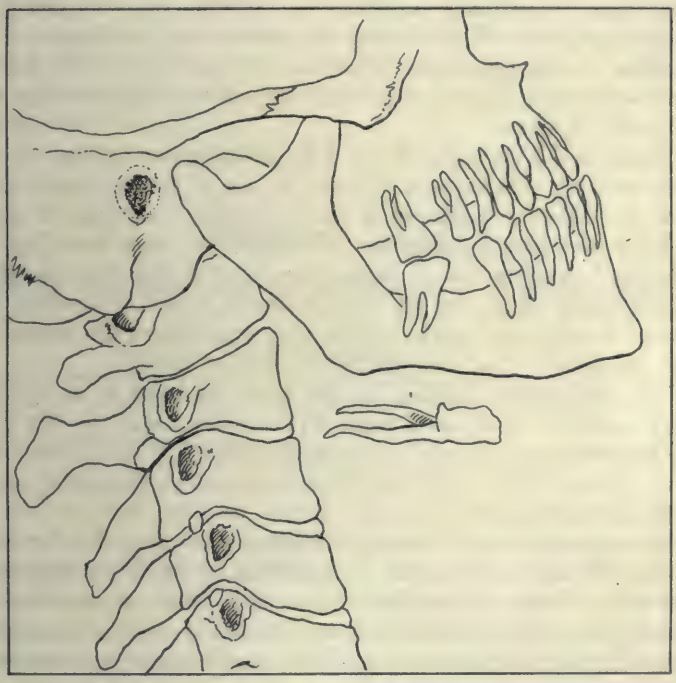


Diagram of the normal skull and spinal column in place.

history is obscure, but the patient was a sailor, who continued at his work. He died as the result of an accident, and the autopsy was carefully reported.

Debenham and Hutchinson[2] reported a most important case of a man who dislocated the atlas and sustained a fracture of the odontoid process of the axis, and yet lived two years. The diagnosis was confirmed by autopsy. The atlas with the included odontoid process was dislocated half an inch forward and a little to the left

[1] Edinburgh Medical Journal, 1839, vol. li. p. 563.
[2] Report of London Hospital, 1867, 1868, vol. iv. p. 210.

side. The odontoid process had been broken through the base, and was ankylosed to the atlas and to the front of the axis in its new position. The lower articular parts of the atlas, pushed forward and downward, were ankylosed to the front surfaces of the axis, and the axis and third vertebra were also ankylosed. The displacement of the atlas forward was such that its posterior arch crossed the spinal canal and left the greater part of the canal behind it. The portion of the canal in front and through which the cord passed did not admit the tip of a child's little finger. It measured the third of an inch from behind forward and three-quarters of an inch from side to side. The cord must have been much compressed. This patient was eventually paralyzed in motion and sensation, but only gradually so. The clinical report was very inadequate. It is likely that the displacement, after the original injury, did not take place all at once, but by degrees, thus leaving the cord to adjust itself to the pressure.

Wyman[1] had a specimen from a dissecting-room subject of whose history nothing was known. It was a case of fracture and dislocation of the anterior fragment of the axis, with ankylosis of the axis and third and fourth vertebræ. Evidently of long standing.

Stimson,[2] quoting Gurlt, recognizes that fracture of the atlas is not necessarily fatal, for in Gurlt's eleven cases immediate death occurred in only two cases, and in only two others did death occur within an hour. One case survived thirteen days.

As to *dislocation*, falling of the head forward is a symptom. Coste's patient lived more than five months, and yet the spinal canal was reduced to a slit 5 mm. wide on the left and 2 mm. on the right. (Coste's case is reported in the *Journal de Bordeaux*, August, 1852; not attainable.)

Stimson speaks of a "bilateral dislocation in opposite directions," in which one articular surface is displaced forward and the opposite backward. This displacement can exist without causing compression, although in Sédillot's case,[3] which is cited as an example, the patient died in seven weeks with symptoms of compression.

Phillips reports a case[4] in which the posterior arch of the atlas was broken off and remained in place, while the anterior portion, carrying with it the fractured odontoid process, was displaced so that it lay entirely in front of and became united with the body of the axis. The patient survived forty-seven weeks.

In Dubreuil's case the patient lived until the seventh day; in Gibson's case until the seventh day. Stimson calls attention to the falling forward of the chin on the chest, and to prominence in the pharynx, and deformity at the back of the neck.

Scudder[5] says that by palpation through the mouth the bodies

[1] Boston Medical and Surgical Journal, 1862, vol. lxv. p. 333.
[2] Fractures and Dislocations, 1899.
[3] Gaz. med., 1842, p. 776.
[4] Med. Chir. Trans., vol. xx. p. 78.
[5] Treatment of Fractures, Philadelphia, 1903.

of the cervical vertebræ may be felt as low as the fifth cervical vertebra. He also says that unilateral dislocation is the most common form, one articular process slipping over and in front of the one below. This causes the head to tilt and rotate.

The above cases do not by any means exhaust the literature of the subject, which is quite extensive, as may be seen by reference to the *Index Catalogue*. Most of the literature, however, refers to cases which have been immediately or quickly fatal, and these of course are the most common. I have thought it worth while merely to collect a few cases in which the patients have survived the accident for a comparatively long time.[1] The opinion that a dislocation of the atlas, as a result of accident, is necessarily quickly fatal, is thus seen to be erroneous. No reference has been made here to cases of caries of the bone, causing displacement, a quite well-known instance of which is related by Mr. Hilton in his treatise on *Rest and Pain*.

VENEREAL WARTS.

THEIR ETIOLOGY, PATHOLOGY, DIAGNOSIS, AND TREATMENT.

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Various terms are in use to designate this pathological condition. A tolerable acquaintanceship with them may prove helpful to the student of venereal diseases. The following serve as examples: verrucæ venereæ; verrucæ of the penis; excrescences; warts; cutaneous tumors; papillomata; condylomata; sycomata; vegetations; venereal vegetations; papillary excrescences; papillary fibromas; acuminate warts; multiple pointed condylomata; *Feizwarzen* ("fig warts"); *Feuchtwarzen* ("moist warts").

The origin of these terms is not definitely known. However, it is fair to assume that the nature and character of the growths, as well as their common seat, gave to them "a local habitation and their name."

Definition. Moist or dry papillary overgrowths, varying in size and number, acuminate or flattened, sessile or pedunculated, appearing usually upon the mucocutaneous surfaces of the male and female genitalia. They are also found upon the scrotum, and

[1] Other references are: Shaw, Med. Chir. Trans., vol. xxxi. p. 289; Lawrence, ibid., vol. xiii. p. 387.

occasionally around the anus. On mucous surfaces they are moist; on skin surfaces they are dry. They are almost invariably multiple, and they may be either venereal or non-venereal.

Historical Note. Venereal warts are not mentioned in the genuine works of Hippocrates. Liston, as well as Celsus, describes them minutely. John Hunter believed them to be syphilitic in origin. In Van Buren and Keyes' first book—the pioneer work on this subject—venereal warts are given due consideration. In the older works on surgery they are often described as a manifestation of syphilis.

Fig. 1.

Large, multiple condylomata acuminata ("papillofibromata") of the human penis; sessile, confluent, and completely filling the coronary sulcus, forming a so-called "collarette." The glans penis is free from growths, and a large drop of gonorrhœal pus is seen oozing from the meatus. Even the keratinized acicular tips of the growths are recognizable and appear of a darker shade than the surrounding tissues. (Photograph by Dr. John S. Fulton.)

Occurrence and Frequency. Age is no factor in the production of venereal warts. They are frequent in children and in pregnant women suffering from irritating discharges—urethral or vaginal. They occur oftenest, however, in young adults of either sex, ranging in age from fifteen to twenty-five years. In the subjoined lists the youngest is fifteen, the oldest thirty-eight.

In males, though they are largely subpreputial—the mucous surface of the prepuce, the coronal sulcus, and sulci of the frenum being their favorite seats—they may occur anywhere on the preputial fold. Warts are also encountered on the surface of the glans and less frequently upon the lips of the meatus. According to Valentine, "they begin in the sulci at either side of the frenum and in the sulcus behind the corona with equal frequency." As stated above, they are also found, though rarely, upon the scrotum and about the anus.

FIG. 2.

Human penis, showing multiple pointed condylomata, aggregated into large masses, pedunculated and springing from the coronary sulcus, as in Fig. 1. A few isolated warts are also seen scattered over the mucous lining of the prepuce. The surfaces of the tumor-masses have lost their cauliflower-like appearance because of compression by the foreskin. (Photograph by Dr. John S. Fulton and Mr. John Johns.)

In the female they originate at the entrance of the vulva, on the carunculæ myrtiformes, the nymphæ, the fourchette, at the introitus vaginæ, at the meatus urinarius, on the skin of the perineum and around the anus. Keyes, in his recent book, states that "venereal warts are found in greatest luxuriance within and around the vulvæ of pregnant women affected with irritating discharges—discharges not necessarily venereal in any sense."

In either sex they may be situated in the urethra and inferior part of the rectum. Oberländer describes a condition of papillomatous

urethritis. Like subpreputial warts, these intraurethral growths vary greatly in size and number. There may be a few near the meatus, or many sprinkled along deeper in the canal. Since the introduction of the urethroscope urethral vegetations have been shown to be not so rare as was formerly believed. They may be sessile or pedunculated and grow from any portion of the canal, but their commonest seat is in the navicular fossa and behind strictured portions of the urethra, springing from the floor. They may attain a size sufficient to obstruct the outflow of urine. Usually, however, they are small and occur in the first inch of the urethra. John Hunter, in all his examinations of dead bodies, saw only two instances of intraurethral papillomata, and these were in very old strictures, where the urethra had suffered considerably. Hunter made the assertion that he had never met with urethral vegetations in women, whilst Ricord said that they are more common in women than in men.

Acuminate condylomata abound around the anus in anorectal gonorrhœa and in untidy females who allow the parts to reek with acrid secretions and irritating discharges. In the appended list of eighteen cases of venereal warts occurring in the out-patient department of the City Hospital there is one example of condylomata of the anus. In this instance—that of a male negro—the rectum was funnel-shaped and there was a slight grayish-white issue, but the gonococcus was not demonstrated.

As to the frequency of venereal warts there is a dearth of statistical evidence bearing upon this point. In the most recent 1800 cases of venereal diseases treated in the out-patient department of the City Hospital, under the supervision of Dr. A. Samuels, venereal warts occur eighteen times or in 1 per cent. of the cases. This, I think, is placing the estimate a little too low. Two per cent. would probably be more nearly correct. An epitome of these cases may be appreciated. Only the salient points are presented. (See Table I.)

Occurrence in Animals. Papilloma of the penis is not restricted to man. It occurs in the equine family, notably the horse. Ruminants are peculiarly exempt. In horses it takes on more closely the character of a true wart of the skin or mucous membrane. I have seen it a number of times. These papillomatous projections are usually observed on the inner surface of the sheath, on the foreskin, and behind the glans—oftenest, however, on the upper and inner surface of the sheath. They are largely due to uncleanness and excessive moisture resultant from neglect on the part of the farrier. They are usually sessile, and occur as a rule in clusters or groups resembling, on a small scale, the "corymbose" variety of smallpox. Youatt, in his excellent treatise on *The Horse*, thus describes them: "These (warts) are tumors of variable size, arising from the cuticle, and afterward connected with the true skin by

means of the vessels which supply the growth of the tumors. They are found . . . on the penis and the prepuce." Left alone and neglected, condylomata about the sheath or penis of the horse sometimes become carcinomatous during the age of physiological decline. At least one such instance has come under my observation. So far as I know, papillary growths of the penis are not found in other of our domesticated animals. Dogs, however, are subject to them. Ashmont says: "Not infrequently as the result of balanitis, warts or vegetations appear on the genitals of dogs. Other causes have been assigned, but in this situation they are doubtless induced by irritating discharges. They may exist as a single excrescence or as a group of several united."

Etiology. The causes of venereal warts are predisposing and exciting. The most important predisposing cause is a long, tight foreskin. Some persons exhibit a constitutional tendency toward these warts. Uncleanliness and maceration of their seat, the presence of an irritating discharge, and balanoposthitis are the usual exciting causes.

Hunter believed in the specificity of venereal warts. Ricord dissented and said: "As to the special cause which excites and keeps up these vegetations, it cannot be sought for in the virus of syphilis." Modern authorities hold to the opinion that the determining factors in the production of venereal warts are uncleanliness and irritation, as in gonorrhœa or balanitis. In persons suffering from herpes præputialis or chancroid they are by no means uncommon. Certain it is that an elongated, phimotic prepuce, replete with retained and decomposing secretions, furnishes an ideal field for the development and growth of these papillary excrescences; and the combined influence of uncleanliness and the irritation produced by a gonorrhœal discharge is the usual *raison d'etre.* Of the eighteen cases of venereal warts (see Table I.) treated in the out-patient department of the City Hospital, seven, or nearly 40 per cent., showed no evidence of venereal disease, while the remaining 60 per cent. were directly traceable to it. The classification of these latter cases is as follows: complicating gonorrhœa, 4; chancroidal ulceration present, 2; chancre and phimosis, 1; history of syphilis, 1; herpes præputialis, 1; suppurating bubo, 1; proctitis (warts of anus), 1. The case listed as occurring with "suppurating bubo" probably should have been placed in the first category—the non-venereal cases. The patient, a young negro above the average intelligence of his race and a medical student, emphatically stated that he never had had any venereal disease and that the warty growths were the cause, *and not the effect,* of the suppurative lymphadenitis. To recapitulate: In each of the non-venereal cases the foreskin was redundant and tight, and the glans was thus kept in an unduly moist state. In the venereal cases it is to be noted that an irritating discharge, gonorrhœal or other, was either present or had

existed at a time coeval with the first appearance of the warty growths. They may be caused, though rarely, by prolonged contact with secretions emanating from mucous patches within the cavity of the prepuce.

Quite recently in my private work there occurred five cases of venereal warts. Three were complications of gonorrhœa, while in the others there was no history of venereal disease. In one of the cases the warts, varying greatly in size, were very numerous, abounding at the meatus, on the glans penis, upon the mucous and cutaneous surfaces of the prepuce and within its cavity, in the coronary sulcus, and in the sulci of the frenum. In three of the cases the warts were few in number and occurred in the sulci of the frenum. In the fifth case the warts, numbering but three, were located on the mucous surface of the prepuce. Table II. is a tabulation of these cases.

So far as is definitely known, venereal warts are neither infectious nor contagious. Ricord says: "The assertion that they are contagious, advanced by some persons, is false." White and Martin, than whom there are no greater authorities, say: "Proof as to the contagious nature of discharges from venereal warts is still wanting, though there are many recorded cases of condylomata developing apparently as the result of contagion." The clearest and best exposition of this phase of the subject is that by Taylor in his *magnum opus*. He mentions the following seemingly convincing instances: Güntz, of Dresden, reported the case of a child who contracted these growths from having used repeatedly the same chamber as its nurse, upon whose genitals at the time innumerable vegetations were seated, and quotes the so-called successful vaccinations of Dr. Kranz in Lindwurm's clinic. Güntz further quotes the case of Sir Astley Cooper's assistant, who, during the ablation of a large condylomatous growth, was wounded in the vicinity of the fingernail. As a result there was developed at the point of injury a growth of condylomata acuminata. In six experiments conducted by Güntz himself, vegetations were removed from the genitals and placed in incisions on the arms, in each instance with a negative result. The late Prof. Petters was the chief opponent of the doctrine of the contagiousness of venereal warts. His exhaustive essay contains the details of twelve carefully conducted but negative experiments. Taylor summarizes thus: Hebra disbelieved in the contagiousness of these lesions, and Ricord was of the same mind. Reder considers the contagion probable, while Geigel regarded it as certain. Zeissl admitted their contagiousness, and Neumann, while conceding the possibility, was in doubt. Lebert, on the contrary, gives it as his opinion that these growths are positively not contagious.

Oberländer does not believe that pointed warts under the prepuce or in the urethra are due to gonorrhœal infection, yet he does consider them contagious. The late Professor Rohé considered their origin by contagion as probable, but not absolutely demonstrated.

To conclude: Concerning the etiology of condylomata it may be said that a long foreskin is the most frequent and most important predisposing cause. Uncleanliness and undue moisture, combined with an acrid, irritating discharge—usually gonorrhœal—are the exciting causative factors in 60 per cent. of the cases; the remainder, 40 per cent., are non-venereal and are due to uncleanliness and maceration of their seat alone. They are essentially inflammatory. The frequent presence of a balanoposthitis or its history, as well as the microscopy of the growths themselves, is, I think, incontrovertible proof of the truthfulness of this statement. The question as to their infectious or contagious nature is still *sub judice.*

Pathology and Histopathology. Condylomata, when small, appear as hyaline spots, often highly vascular and composed largely of epithelium. They may be discrete or confluent, sessile or pedunculated, single or branched. Viewed grossly, they may be cauliflower-like in appearance or form aggregations resembling a cock's comb. Their delicate structure, as well as their exposed situation, renders them extremely liable to injury, and on account of their excessive vascularity they are prone to bleed profusely on the slightest provocation.

Histopathologically, venereal warts are true papillomata. They consist of a framework of connective tissue covered by stratified epithelium. The connective-tissue stroma is quite vascular, and the epithelium usually of the squamous type. They are due to "hypertrophy of the papillary and mucous layers of the skin; at the same time there is a corresponding development of bloodvessels." Papillomata are of two kinds—epithelial and fibrous—and, as Guiteras says: "It is frequently impossible, owing to coincident hyperplasia of the connective tissue, to separate epithelial from fibrous papillomata. Many papillomata are inflammatory, and are best classified as *hypertrophies,* being due to irritation."

One of the earliest descriptions of the histology of venereal warts is that by M. Lebert. He speaks of them as "nothing else than a development of the papillæ of the epidermis." Hunter and Ricord describe them minutely; likewise Virchow in his *Cellular Pathology.* Weichselbaum, quoted by Valentine, described a condylomatous excrescence as a "simple or branched papilla, built on the type of a skin or mucous papilla, and covered with epithelium of varying thickness. The connective tissue in these papillæ is generally much richer in cells and vessels than is the connective tissue of the base from which they spring. The epithelial covering can be materially thicker than that of the region from which it originates, but ordinarily it has the usual character of the epithelium of the region. The papillomata proceed from normal papillæ of the skin or mucosa, which enlarge; new formation of papillæ also takes place."

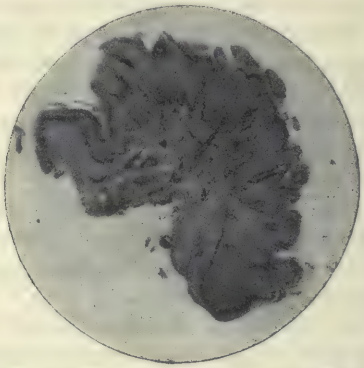
Unna does not regard condylomata as true papillomata, and contradicts the latter statement of Weichselbaum, inasmuch as he says

there is not any independent growth of the papilla in condylomata, but only an increase of their size from infiltration with leukocytes. To the infolding of the proliferating epithelium upon the papillæ, Unna attributes the apparent increase in their number.

Stengel, Green, Delafield, and Prudden, and other recent pathologists, describe condylomata—"venereal warts." Delafield and Prudden define them as "hypertrophied papillæ covered with epithelium."

The writer has studied carefully numerous microscopic sections of venereal warts, cut in divers directions and from different parts of the growths, and stained by a number of the most approved meth-

Fig. 3.



Microscopic section of "papillofibroma" of human penis, shown in its entirety. At the lower left-hand margin may be seen a small area of normal skin—truly a striking contrast. In close proximity to the outskirts of the specimen are tips of papillæ, cut transversely. The acuminate extremities of the subdivisions of the growth stand out in bold relief, and the vessels of the corium are congested. The surface-layers of epithelium have undergone keratohyaline degeneration. The structure is epithelial and fibrous tissues in almost equal proportions. × 23. (Photomicrograph by Dr. John S. Fulton and Mr. John Johns.)

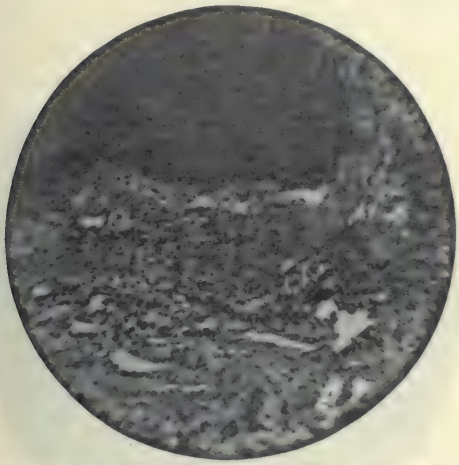
ods. A detailed account of the most striking results obtained, arranged under two headings, "Tissue Stains" and "Bacterial Stains," will next be given:

1. *Tissue Stains.* (*a*) Stained in the regulation way with eosinated logwood, it is next to impossible to conceive of a more beautiful picture in pathological histology. The epithelial and fibrous strata seem about equally divided, and between the two there is a zone rich in adenoid tissue and resembling histologically the basement membrane of the stomach mucosa. The relation between stroma and epithelium can be seen even with the naked eye. Seen in its entirety with a very low-power lens (Fig. 3), the contour of a typical branch of one of these growths is not unlike that of a normal papilla of the skin or tongue.

Epithelium. Under the low power the most striking change consists in a perceptible thickening of the epithelium, which seems to

affect all of the strata equally. The papillæ and the interpapillary connective tissue show a great increase in length and thickness. That portion of the corium adjacent to the deepest layer of epithelium shows a distinct zone of cellular infiltration, and the vessels of the corium show some congestion. Under a higher power the thickening of the epithelial layer seems to be due, at least in part, to actual increase in size of the individual epithelial cells. This is especially noticeable in the prickle-cell layer of the rete Malpighii, a condition first described by Dürck and later observed independently by the present writer. Here the nuclei are swollen and often surrounded by a clear, œdematous vacuole and the cytoplasm is also swollen and at times pale and œdematous.

FIG. 4.



Microscopic section of "papillofibroma" of human penis. There is a pretty sharp line of demarcation between the epithelial covering and the connective-tissue framework. A layer rich in cells and resembling lymphoid tissue is seen immediately beneath the deepest layers of epithelium. At no place has the epithelium invaded the connective tissue—a point to be borne in mind in differentiating from epithelial carcinoma. × 745. (Photomicrograph by Dr. John S. Fulton and Mr. John Johns.)

There are certain cells in this region which almost resemble parasites. These are about the size of a red blood corpuscle, possess small round or elongated, darkly staining, often irregular nuclei, and are surrounded either by a clear vacuole or by a minimal amount of eosin-staining protoplasm. In addition to hypertrophy of the individual cells there is also evidence of hyperplasia or numerical increase. This is proven by the presence of a moderate number of karyokinetic figures indicating rapid multiplication by indirect cellular division.

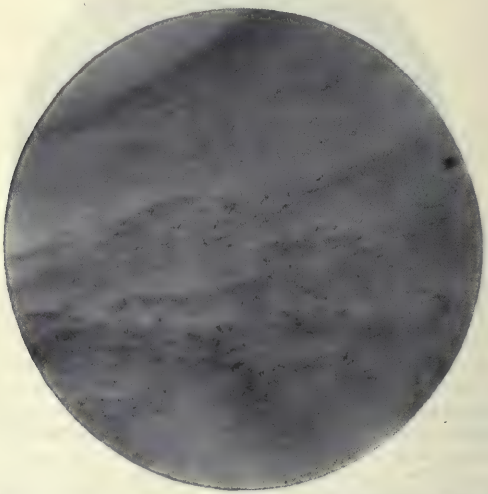
Corium. The intercellular lymph spaces are distended by cells of various types. There are a few polynuclear leukocytes present, but the exudation is mainly made up of small mononuclears or

lymphocytes and proliferated endothelial cells. This cell accumulation is particularly marked at the bases of the papillæ, in the perivascular lymph spaces surrounding small nerves. There are also present a few large lymphocytes or "highly vacuolated plasma cells of Waldeyer."

(*b*) With Van Gieson's stain the connective tissue of the corium is well shown, and it can be traced as fine strands into the connective tissue of and between the papillæ.

(*c*) Sections stained in polychrome methylene blue (Unna's) show a number of plasma cells, but no *mastzellen*. These cells, described by Unna and occurring in subacute and chronic inflammatory processes, are not identical with the plasma cell of Waldeyer alluded to above. The protoplasm stains violet blue and there are no distinct granules.

Fig. 5



Section of "papillofibroma" of human penis stained by the Gram-Weigert method. Bacteria (cocci, diplococci, and bacilli) are demonstrable lying in and among the epithelial cells. Darkly-staining plasma cells and a limited number of leukocytes are seen in the peripheral portion of the corium. × 1000. (Photomicrograph by Mr. John Johns.)

2. *Bacterial Stains.* Sections of specimens of venereal warts hardened in alcohol were next stained for bacteria. The methods employed are: Gram's, Gram-Weigert's, Stokes' modification of Gram-Weigert's, and the tubercle-bacillus method.

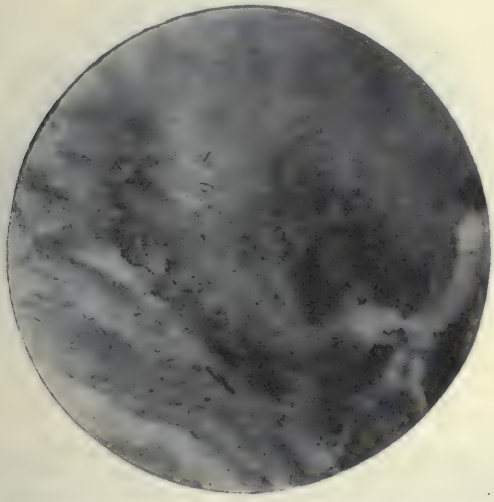
(*a*) *The Gram Method.* Large numbers of Gram-staining bacteria—cocci, diplococci, and bacilli—are to be seen. These will be described in the succeeding paragraphs.

(*b*) *The Gram-Weigert Method.* On staining sections by Weigert's method, masses of bacteria could be seen, even under the low power. These bacteria are limited to the stratum corneum or

scaly layer of the epidermis, and cannot be found in the adjacent stratum lucidum or granulosum. Under the oil-immersion lens they consist mainly of micrococci and diplococci, but a few fine, long bacilli can also be distinguished. These bacteria are strictly limited to the surface and do not invade the deeper layers of the epidermis. They seem to be distributed in greater or lesser numbers throughout the entire superficial horny layer of the skin.

(*c*) *Stokes' Method.* This is a modification of the Gram-Weigert method. It was first described by Dr. William Royal Stokes in his paper on "Ulcer of the Stomach Caused by the Diphtheria Bacillus," published in the *Johns Hopkins Hospital Bulletin*, July, 1901. The preliminary staining with hæmatoxylin has been dispensed

FIG. 6.



Magnification and specimen same as in Fig. 5, showing numerous micrococci and bacilli in the superficial layers of the epidermis. × 1000. (Photomicrograph by Mr. John Johns.)

with, and the method now simply consists in first staining the section in 1 per cent. watery eosin, and then decolorizing with water. The section is then stained by the usual Weigert method.

When the sections are stained by Stokes' modification of Weigert's method, similar bacteria to those described above can be made out. This process serves as a good histological stain as well as a bacterial stain, and in my experience has given better results in routine work than the preliminary staining with carmine.

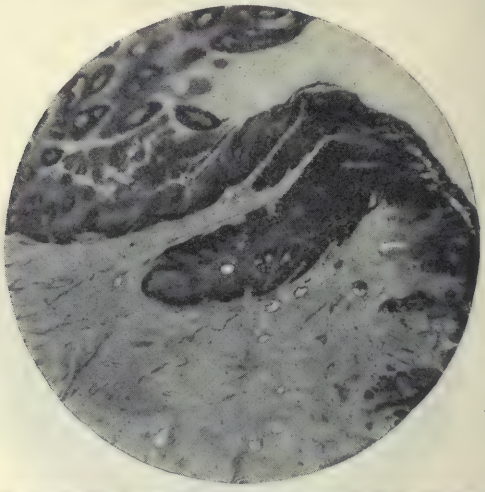
A method almost identical with the above has been used quite extensively in the Pathological Division of the Bureau of Animal Industry, United States Department of Agriculture. In this well-organized department, bacteria as well as sections of tissue are not infrequently stained by Gram's method, or Gram-Weigert's method,

and followed by, or counterstained with, eosin. In Stokes' modification the staining with an aqueous solution of eosin precedes the Gram-Weigert method.

(*d*) *The Tubercle-bacillus Method.* No bacteria were demonstrable in sections stained by the Ziehl-Neelson-Gabbett method.

Histopathology of Papilloma of Horse's Penis. The changes in the epithelium do not differ materially from those described above in the human cases, but the cellular infiltration of the corium presents a complex study. In the first place, the tissue is richly infiltrated with proliferated, elongated connective-tissue cells; but, in addition to this, there are greatly increased numbers of large and

FIG. 7.



Papilloma from the penis of a horse, showing the hyperplasia producing great elongation of the papillæ and the loose fibrous tissue of the corium beneath. The upper portion of the photomicrograph shows a sulcus containing many exfoliated superficial epithelial cells. × 23. (Photomicrograph by Mr. John Johns.)

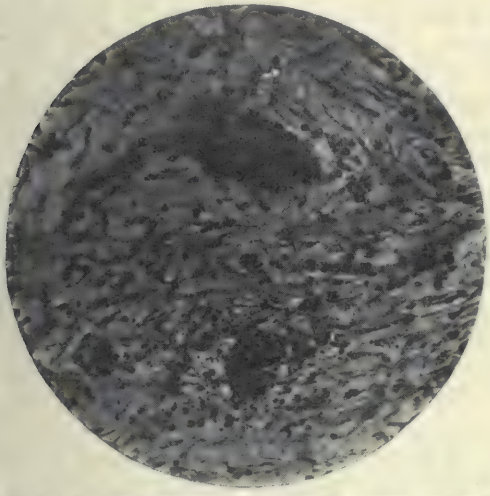
small lymphocytes. The large lymphocytes often have their nuclei eccentrically placed, resembling the so-called plasma cells. Both the large and small lymphocytes are found in excessive numbers in the lymphatic spaces and in the capillaries, and they doubtless wander from the bloodvessels into the surrounding tissues. The crowded condition of the lymphatics is probably due to the absorption of these cellular elements from the tissues. There are a few eosinophiles scattered through the corium. The corium presents a rather loose, myxomatous appearance, and the lymph spaces are often perceptibly distended. The interpapillary connective tissue—of which the papillæ of the true skin is a physiological prototype—contains many large and small lymphocytes.

SYMPTOMATOLOGY. There is no definite symptomatology peculiar to venereal warts. The patient may complain of a disagreeable

sensation—a sense of "fulness"—or a feeling of discomfort about the parts, and much smegma and a peculiar, sickening odor are usually in evidence, especially when the warts are very numerous. Unless infection, with subsequent ulceration, takes place, these warty growths are attended with but little, if any, pain. Even when acutely or subacutely inflamed, pain is not a prominent symptom. Specimens from one of my cases show a subacute inflammatory process; yet there was no pain connected with it.

In women condylomata give rise to "itching, burning, and a general feeling of discomfort, but otherwise do not cause symptoms." Stoner reports a case in which numerous condylomata

Fig. 8.



Specimen same as Fig. 7. This picture shows the myxomatous fibrous tissue which forms the base of the tumor. The connective-tissue cells, with their wavy distal filaments, are well shown. The lymphatic capillary contains numerous lymphocytes, which are also scattered throughout the tissue as so-called plasma cells. A capillary bloodvessel, filled with red blood cells and containing a few lymphocytes, is also seen in the upper portion of the picture. × 745. (Photomicrograph by Mr. John Johns.)

studded the surface of the vulva and vaginal walls, a large mass occupied a site adjacent to the anus, and several occupied the cervix uteri. A profuse gonorrhœal discharge from the vagina and urethra was present, but there were no subjective symptoms. I have seen an analogous case. Excluding the mechanical inconvenience, the affection was symptomless and painless.

The symptoms of intraurethral papillomata next merit brief discussion. These are usually slight. There is a thin, mucopurulent discharge, chronic from the first, with slight burning during urination. When they attain large size, or grow upon the meatus, they may interfere with urination and ejaculation. Often there is free bleeding on instrumentation.

Morrow, in a recent article on "Growths of the Male Urethra," says: "Symptoms depend somewhat on the size and location of the growths, those of the anterior urethra producing points of tenderness, gleety discharge, obstruction, and urethral hemorrhage; in the posterior urethra they cause hæmaturia, urethral hemorrhage, sexual hyperæsthesia, prostatic enlargement, frequent micturition, incontinence, and obstruction."

Diagnosis. (*General and Differential.*) By simple inspection the diagnosis of venereal warts can usually be established beyond peradventure. Papillary excrescences, cauliflower-like and appearing on the moist mucocutaneous surfaces of the external genitalia of young persons of either sex, are almost invariably *verrucæ venereæ*. An impure connection or the history or presence of a venereal disorder is not a *sine qua non*. By reason of pressure inflicted by a tight foreskin, and sometimes as a result of the use of cauterants, their exterior is very materially altered. Instead of their pristine cauliflower-like appearance they become much flattened, coarser, and denser looking. Even then the history, seat, and mushroom-like appearance of the growths are almost certainly sufficient for their intelligent identification.

The diagnosis of intraurethral papillomata is made by distending the meatus with the thumb and finger, when one or more warts may usually be seen at or just within the meatus. When more deeply seated, the endoscope and bulbous bougie are valuable diagnostic aids. The tendency of these growths to bleed on the slightest touch compromises the usefulness of the endoscopic tube. By deeply inserting a bulbous bougie of fair size and with shouldered acorn tip, and making pressure externally over the course of the urethra just in front of the shoulder of the instrument as it is withdrawn, fragments of the warty growths will be found upon this shoulder, and hemorrhage from the urethra will follow (Keyes).

For the sake of perspicuity I shall make brief allusion to the principal conditions from which *verrucæ venereæ* must be distinguished. These are: "condylomata lata," or syphilitic warts, epithelioma, mucous patches, urethral polyps and urethral caruncle when occurring in the urethral canal, and hemorrhoidal tumors when found about the anus or rectum.

In condylomata lata, or syphilitic warts, other manifestations of the disease are present, and a history of syphilis can usually be elicited. Only in long-standing cases, in which the external appearance of the warts is altered—when they are broadened by growth—is such an error in diagnosis likely to be made.

Epithelioma in its incipiency may be mistaken for condyloma. The patient's age, the presence or absence of infiltration of the base of the tumor, or tumors, and the surrounding tissues, and the condition of the neighboring lymph nodes are the most important differential points. The former—epithelioma—appears late in life and

is accompanied by infiltration of the surrounding tissues and involvement of the anatomically related lymph glands; in the latter—condyloma—these features are conspicuous by their absence, excepting as rare complications. However, as a precautionary measure, a wart appearing on the penis after middle life should be excised and subjected to careful scrutiny by a competent pathologist and microscopist.

Condylomata may be confounded with mucous patches. This can only occur when the former are flattened and macerated by free secretion or discharge. A history of lues, the pearly lustre of the mucous plaques, and the concomitant symptoms determine the diagnosis.

Differentiation from polypoid growths of the urethra and from urethral caruncle is of but slight import, as the treatment of these conditions is similar, namely, surgical removal. In condylomata, as previously stated, the urethroscope is of but little avail, because of the hemorrhage which ensues. Condylomata here as elsewhere are almost invariably multiple and are found oftenest in the anterior urethra. In one of Morrow's cases "twenty were removed by the snare, one came away spontaneously, and an interminable number were removed by the caustic solutions." Polypi—fibrous and mucous—are usually single and occur, as a rule, in the posterior portion of the urethra. They are not nearly so vascular nor sensitive as the multiple pointed condylomata. To employ the phraseology of Keyes, urethral polyps "do not bleed on contact with an exploring instrument, their only symptom being a slight urethral discharge and perhaps diminution in the size of the urinary stream, with some real or fancied urethral neuralgia."

Urethral caruncle is almost unknown in the male urethra. In the female it produces painful micturition—sometimes excessively so—vaginismus, and dyspareunia. Urethral caruncle is situated at the edge of the urethral mucous membrane and is slightly elevated above the surface. It is deep red in color, granular in appearance, and exquisitely sensitive. "Urethral polypus is non-sensitive, has a longer pedicle, and is usually attached higher up in the urethra" (Davenport).

Condylomata abounding about the anus and in the lower part of the rectum as a result of anorectal gonorrhœa may be confused with hemorrhoids. The differential diagnosis, however, is quite simple. "Hemorrhoids are either round, pendent tumors, or loose folds of the integument, having a smooth surface; whereas condylomata are flat and possess an irregular, warty appearance" (Agnew).

Prognosis. The prognosis as to the early disappearance of the warts is good. Regarding permanency of cure it must be said that recurrences are not infrequent. Unless the exciting cause be removed, the warts are extremely likely to return, and often more abundant than at first. Thorough eradication of the growths

themselves, and cauterization of their base, combined with removal of the etiological factor or factors, are the only measures that afford lasting relief. However, I cannot speak definitely regarding the frequency of return of these growths, nor are statistics relative to this point at my command. In Table I. there are chronicled three recurrences—a proportion of $\frac{1}{6}$ or $16\frac{2}{3}$ per cent.

The prognosis of intraurethral papillomata is unfavorable. Keyes states that "the malady may last indefinitely, individual warts disappearing to be replaced by others." Oberländer cites a case of warts in the urethra of a patient who had had a discharge for twenty years.

Complications and Sequelæ. Phimosis, paraphimosis, balanitis, and balanoposthitis are the commonest complications. Oftentimes, however, these conditions are due to the gonorrhœa which has caused the warts rather than to the presence of the warts themselves. As stated in a previous paragraph, a balanitis or a balanoposthitis is, in 40 per cent. of the cases, a forerunner and not a consequence of a crop of venereal warts. Inflammatory bubo, either suppurative or non-suppurative, sometimes results. Case XV., Table I., is an example of suppurating bubo complicating warts. Occasionally warts themselves become infected and undergo suppuration and ulceration. Even gangrene is a possible complication. Both Valentine and Taylor speak of it. A young man with a very prolific growth of warts of the penis, complicated by a paraphimosis, suppuration of the warty growths themselves, and a gangrenous area on the under surface of the constricted portion of the foreskin, was quite recently exhibited at Professor Bevan's clinic. He had suffered a severe and prolonged attack of gonorrhœal urethritis, and some discharge was still present.

Perforation of the prepuce sometimes results. Taylor mentions it. I have seen it once. Three years ago a middle-aged man was admitted to the surgical ward of the City Hospital with a fractured femur. He had an old healed perforation of the prepuce of considerable size, which he informed me resulted from sloughing of warts which he had had when a young man. In Morrow's intraurethral cases their presence produced dilatation of the urethra and prostatic enlargement. Anon they engender a chronic urethritis, and Hunter speaks of stricture being caused by them.

Malignant degeneration—the implacable aftermath of so many tumors primarily benign—may take place in persons beyond middle life, but such a consequence must be exceptionally rare. In two cases of epithelioma of the vulva with which I was conversant, the probable history in each case was that of long-standing condylomatous excrescences which had become malignant. Keyes amplifies the foregoing when he says that "warts and chronic balanitis are the most fruitful sources of epithelioma, the former especially if neglected and allowed to remain foul and moist." Kaufmann,

quoted by Keyes, collected thirty-three cases of epithelioma of the penis. Twenty-nine of the thirty-three began as apparently benign warts.

According to Keyes, implantation warts—warts occurring after circumcision—are especially liable to hypertrophy and become horns. Sterility, due to organic impotence, may result, the warts acting as a mechanical impediment to the performance of coitus.

PROPHYLAXIS AND TREATMENT. The prophylaxis and initial treatment of venereal warts are to all intents and purposes one and the same. In either instance, after cleanliness, the golden rule is, *remove the cause.* If a gonorrhœa exists, treat it by the latest and best methods. If there be a long foreskin, with accumulation of secretions, circumcise. If phimosis is present, a dorsal incision may be necessary. If a balanitis or a balanoposthitis, repeated cleansing and drying of the parts should be enjoined. These, combined with the intelligent use of some simple dusting powder, will generally be all-sufficient.

The treatment proper of venereal warts may be either medical or surgical. The former includes topical applications of the various dusting powders, ointments, lotions, pastes, and caustics. The second resolves itself into complete riddance of the parts of growths by means of the knife, scissors, or curette—preferably the scissors or the sharp spoon. Perhaps the use of caustic agents should be placed also under this caption.

As a preliminary measure it is expedient that we resort to medical or palliative treatment. The first principles—cleanliness, dryness and removal of the cause—having been faithfully complied with, one of the much-vaunted remedies—and their name is legion—should be employed. The relative merits of these subsequently will be discussed briefly *seriatim.*

Ricord wrote: "At the present day the rational course to take consists in treating the complications, *when such really exist,* and in making local applications to the vegetations as to a local disease. . . . Swediaur's powder is generally inefficacious. We should, in most cases, resort to cauterization, and especially to excision."

Medical Treatment. Dusting with calomel alone is one of the simplest methods of treatment. A dry dusting powder composed of calomel and bismuth—calomel one part, bismuth two parts—will perhaps be more efficacious. A formula in pretty general use in the routine treatment of this class of cases at the out-patient department of the City Hospital is:

℞.—Hydrargyri chloridi mitis . . . . . 1 drachm.
Bismuthi subnitratis . . . . . 2 drachms.—M.
Sig.—Dusting powder.

Dusting the growths with boric acid not infrequently causes their rapid disappearance. Zinc oxide and bismuth, equal parts, has its advocates. A 10 per cent. salicylic acid ointment may prove useful.

Resorcin sometimes supersedes all other local applications. It is thus prescribed at the hospital clinic:

℞.—Resorcini . . . . . 15 grains.
Vaselini . . . . . 1 ounce.—M.
Ft. ungt. Sig.—Locally, after carefully cleansing the parts.

The following mixture is recommended by White and Martin, and a similar one by Keyes:

℞.—Acidi salicylici . . . . . 1 drachm.
Acidi acetici . . . . . 1 ounce.—M.
Sig.—Apply with a brush once daily.

This combination forms a curd-like mixture and will generally remove warts within twelve to twenty-four hours. A sufficient quantity of the dregs should be deposited upon the growths to cover their entire surface, and allowed to dry. One or two applications are usually sufficient. Relapse is said not to occur after this treatment.

In the acuminate form, cleansing, drying, and dusting with powdered savin acts as a direct specific (Posner). Valentine recommends that the mass be touched three times daily with ferric chloride. The shrunken, shrivelled portions should then be curetted and the application repeated, until the base is reached. This must be thoroughly curetted and its bleeding arrested with cotton pledgets soaked in 5 per cent. solution of antipyrin.

Surgical Treatment. Surgical removal of the growths—curettement, extirpation, or excision—undoubtedly furnishes greater assurance of permanent success. This may be effected, as stated above, by means of the curette, knife, or curved scissors.

Neither curettement nor excision is as effectual as removal with the curved scissors. The first, because of its inaccuracy and incompleteness, and the second, by reason of its unhandiness, is to be superseded by a pair of rat-tooth forceps and curved scissors.

Unless the growths are very small and few in number, an anæsthetic, general or local, will be required. Ether, undoubtedly, is the safest and best general anæsthetic. Of the local anæsthetizing agents, ethyl chloride and cocaine stand ahead of all others. Ethyl chloride may be purchased in metallic containers ready for use, and is sprayed over the surface to be anæsthetized. Cocaine, in 10 per cent. solution, is always available and will answer every purpose.

The method of operating on condylomata is as follows: After a thorough cleansing of the diseased area, a 10 per cent. solution of cocaine is applied for five minutes before the operation. When the growths are discrete and small, they are seized, one by one, with a pair of rat-tooth forceps, drawn upward and removed, together with the underlying tissues, by a snip of the scissors. The bleeding points are then cocainized, touched lightly with pure carbolic acid, and dusted with iodoform or some other powder. The application of a gauze bandage completes the dressing.

When the neoplasm has a large base, or is confluent, the projecting mass may be shaved off level with the surrounding surface by means of a sharp, flat knife. The base should be thoroughly curetted, and then cauterized with carbolic or nitric acid. The wound is then dusted with iodoform or with a powder made of calomel and zinc oxide, equal parts of each, and a gauze dressing applied. As in the case of the smaller growths, the bleeding surface should be cocainized prior to cauterization, to render the operation painless. Bleeding, though free for a few moments, usually stops on cauterization, or on the application of a cotton pledget soaked in a 5 per cent. solution of antipyrin. In excising unusually large papillomata the hemorrhage is sometimes alarming. It is well, on such an occasion, to have an actual cautery ready for use in case of emergency. Only spouting vessels should be ligated.

When practicable, a still more radical step consists in cutting away the papilloma and its base entire, approximating the edges of the wound and suturing them. This operation is applicable when the growth, or growths, spring from the prepuce or skin surface.

Treatment with Caustics. The cauterant remedies usually applied are (*a*) nitric acid; (*b*) chromic acid; (*c*) caustic potash; (*d*) silver nitrate; (*e*) carbolic acid; and (*f*) glacial acetic acid.

When nitric acid is the agent employed, the surrounding parts should be protected by some bland ointment, the acid well rubbed in, and an antiseptic dressing applied. The application should be repeated on alternate days until the warts are destroyed.

Chromic acid, though a most excellent caustic, is nevertheless a dangerous one, as toxic symptoms sometimes result, and a few fatal cases are recorded. It should be applied with a camel's-hair pencil, once daily, either pure or in a 10 per cent. solution. Morrow used a solution of chromic acid, 100 grains to the ounce. White and Martin speak very commendably of caustic potash. They recommend its use in the following form:

℞.—Plumbi oxidi		2 grains.
Potass. hydrat.		20 grains.
Aqua	q. s. ad	1 drachm.—M.

Sig.—Shake well, and apply by means of a brush to the lesion, which has previously been cleansed and dried. One or two applications are sufficient.

The silver stick or a solution of silver nitrate, 60 grains to the ounce, may be used for the same purpose; likewise pure carbolic acid or glacial acetic acid.

Treatment of Intra-urethral Papillomata. This is pre-eminently surgical. Caustic applications, however, are sometimes used; but their range of usefulness is circumscribed within pretty narrow limits, and stricture may result.

Intraurethral growths may be removed by means of the urethral forceps, the wire snare, the urethral curette, or the galvanocautery —all through the urethroscopic tube. When located anteriorly, as

is usually the case, after cocainizing the urethra they may be grasped through a meatoscope or dilating speculum by means of forceps or a silk thread. The urethroscope can then be introduced and the deeper growths removed by ligature, the incandescent snare, curette, or galvanocautery. Hemorrhage, which is usually copious and troublesome, may be controlled by direct application to the growths of adrenalin chloride solution, 1:1000. Finally, the points from which the papillomata spring should be lightly cauterized with pure carbolic acid, glacial acetic acid, or a little fused nitrate of silver upon the end of a long probe.

Treatment of Venereal Warts in Women. This is analogous to that in the male, and needs no special elaboration. In Stoner's case the warts were removed under local anæsthesia and their bases cauterized; but they persistently returned. Eventually the warts were removed and their bases cauterized under ether anæsthesia, and a permanent cure effected. Stoner says: "So extensive was the involvement of the labia that much of them had to be sacrificed with the removal of the growths. The canal (vaginal) was loosely packed with gauze and a douche of antiseptic solution was used twice daily."

Intraurethral papilloma is exceptionally rare in women. The methods of treatment are similar but simpler than in the male, owing to the comparative shortness and dilatability of the urethral canal in women.

Treatment of Anorectal Condylomata. Here, as elsewhere, absolute cleanliness is difficult, but essential. If a proctitis exists, antiseptic rectal injections (boric acid, sulphocarbolate of zinc, permanganate of potash, or nitrate of silver) should be enjoined. Dusting the warts with calomel or resorcin, or local applications of resorcin ointment, oftentimes will cure them. When rebellious to treatment they should be removed with the scissors and their bases cauterized with pure carbolic acid.

Conclusions. The following conclusions may be deduced:

1. Venereal warts, so called, are hypertrophies rather than tumors. They are inflammatory, being due to irritation.

2. These papillary overgrowths constitute from 1 to 2 per cent. of all cases of genito-urinary disease; 60 per cent. are venereal and are due to acrid, irritating discharges; the remaining 40 per cent. are non-venereal and are due to uncleanliness and maceration of their seat alone.

3. They are not confined to mankind, dogs and horses also being subject to them. Ruminants are exempt.

4. When small, the best treatment is palliative; when large, they are best removed surgically. Even then recurrences are frequent.

5. The term "papillofibroma" most correctly defines these interesting pathological new-formations.

6. The question as to whether or not venereal warts are infectious or contagious is, as yet, purely a speculative one.

7. Numerous Gram-staining bacteria are seen embedded in the epithelium and in the lymph channels. The demonstration of micrococci and bacilli in these lesions suggests that the hypertrophy and hyperplasia of tissue may be produced by certain irritating products of these bacteria.

Thanks are due Dr. John S. Fulton and Mr. John Johns for taking the photographs and photomicrographs, and Drs. A. Samuels and I. P. Robinson, both of the genito-urinary department, for invaluable aid in the compilation of statistics.

Below is attached a list of the cases referred to in the text. Only the salient features have been tabulated.

TABLE I.

Case.	Age.	Seat of growths.	Treatment.	Result.	Remarks.
1	15	Prepuce and glans penis.	Calomel and bismuth.	Cured.	Complicating gonorrhœa.
2	19	Outer surface of prepuce and coronal sulcus.	Unguentum resorcini.	Cured.	No history of venereal disease.
3	19	Coronal sulcus.	Calomel and bismuth.	Cured.	No history of venereal disease.
4	21	Sulci of frenum.	Calomel and bismuth.	Cured.	History of syphilis.
5	21	Coronal sulcus and glans penis.	Calomel and bismuth.	Cured.	No history of venereal disease.
6	21	Internal surface of prepuce.	Surgical removal.	Cured.	Complicating gonorrhœa.
7	21	Prepuce, inner and outer surface.	Surgical removal.	Cured.	Complicating gonorrhœa.
8	22	Coronal sulcus and sulci of frenum.	Unguentum resorcini.	Improved.	Herpes preputialis also present.
9	22	Coronal sulcus.	Calomel and bismuth.	Improved.	Chancroidal ulceration.
10	22	Coronal sulcus.	Unguenti resorcini.	Cured.	No venereal history.
11	25	Glans penis, coronal sulcus, and sulci of frenum.	Calomel and amylum.	Cured.	No venereal history.
12	25	Glans, coronal sulcus, and sulci of frenum.	Calomel and bismuth.	Cured.	No venereal history.
13	25	Sulci of frenum.	Calomel and bismuth.	Improved.	Chancroidal sore.
14	25	Prepuce, glans, coronal and frenal sulci.	Zinc oxide and bismuth.	Cured.	No venereal history.
15	27	Prepuce, glans, coronal and frenal sulci.	Surgical removal.	Cured.	Suppurating bubo.
16	28	Margin of anus.	Unguentum resorcini.	Cured.	Funnel-shaped rectum; proctitis.
17	32	Coronal sulcus and sulci of frenum.	Unguentum acidi salicylici.	Cured.	Had had gonorrhœa.
18	38	Margin of prepuce.	Dorsal incision; acid boracic.	Improved.	Chancre; phimosis.

TABLE II.

Case.	Age.	Seat of growths.	Treatment.	Result.	Remarks.
1	17	Back of corona glandis.	Surgical removal.	Cured.	Complicating gonorrhœa.
2	19	Prepuce, corona, glans, and meatus.	Surgical removal.	Cured.	Complicating gonorrhœa.
3	22	Left sulcus of frenum.	Calomel and bismuth.	Cured.	No venereal history.
4	24	Right sulcus of frenum	Surgical removal.	Recurrence.	Complicating gonorrhœa.
5	32	Sulcus, left, of frenum.	Unguentum resorcini.	Cured.	No venereal history.

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PNEUMOCOCCUS ENDOCARDITIS.

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THIS subject is not a new one, for the literature upon it dates back to 1835, but it deserves attention, because there has been no extensive review of it since 1885, and since that date our knowledge has increased sufficiently to take the subject from the field of the pathologist and place it in that of the internalist. The subject to which I refer is that of acute endocarditis excited by the pneumococcus

The study of acute endocarditis has passed through the same stages of development shown by many other subjects in medicine. At first the subject attracted only limited interest from the pathologist, and only later and gradually did the subject take on clinical interest. Finally, however, it became possible to build up a sufficiently well-marked clinical picture to enable one to diagnose the condition during life in a certain percentage of the cases.

Efforts at classification of the cases were first based entirely upon the gross appearance of the exudate upon the endocardium, the verrucose and the ulcerative forms, and this classification is still maintained in various places. This is, however, a purely artificial classification, which does not correspond either to the clinical course of the cases or to the etiology.

The words benign and malignant are still frequently used in describing acute endocarditis, and, while they are not scientific, they are convenient, and, roughly speaking, correspond to the verrucose and ulcerative types.

Since the articles by Weichselbaum, in 1886, there has been no question of the fact that the ulcerative endocarditis is due to the action of a variety of bacteria, particularly the streptococci, staphylococci, pneumococci, and gonococci; but the acceptance of the idea that all cases of endocarditis, whatsoever their clinical course or the character of the endocardial exudate, are due to the action of bacteria has been less ready. There is now no reason for questioning this, the only exception to the rule being the valvular changes seen secondary to arteriosclerosis. The time has come for us to adopt an etiological classification for cases of endocarditis, although it must be admitted that demonstration of the bacteria in cases of chronic endocarditis is usually impossible, and often difficult, even in the acute cases. That the causal bacteria may be demonstrated during life in certain cases will be proved by the cases reported here.

The first case which I have to report is as follows:

Grace K., aged twenty-five years, has suffered from cardiac symptoms for about ten years. She has been well up to five weeks ago, when she began to suffer from pains in the muscles generally. The joints were free. Later, cough with mucopurulent expectoration, with dyspnœa on lying down and on exertion. No œdema. Examination shows a small, poorly nourished woman. Slight cyanosis when lying down. Rales irregularly scattered over both lungs. Apex of heart in fifth interspace beyond the nipple line. First tone palpable at apex. Presystolic thrill at apex. Second pulmonary tone accentuated and palpable. The absolute heart dulness extends to the third rib above, half an inch beyond the right border of the sternum and to the apex. Systolic and presystolic murmur at apex. Aortic tones pure. Spleen not palpable. Liver enlarged. Urine normal. Temperature, 101°; pulse, 96; respirations, 32.

Diagnosis. An acute exacerbation of an old endocarditis; mitral insufficiency and stenosis.

The temperature ranged irregularly from 99° to 105.4° for five days, and then returned to normal. Here it remained for four days, when the girl had a chill, and the temperature rose to 104°, and a pneumonia, which eventually involved the right middle and lower lobes, developed. Pericarditis developed as a complication. Pneumococci were repeatedly found in the circulating blood. The temperature fell by lysis, but the pneumococci remained in the blood for ten days after the temperature became normal.

The temperature remained normal for something over two weeks, and the patient had been out of bed for three days, when she complained of feeling poorly, and was found to have a temperature of 99° and a completely developed consolidation of the left lower lobe. The temperature ranged to 102° for two days, but the sign of consolidation persisted for several days.

Eventually the patient recovered, and left the hospital with the same lesion of heart present upon entrance.

It may be objected that the diagnosis of an acute exacerbation of an old endocarditis is not justified in this case, but I believe that the cardiac disturbance, with an irregular temperature, not accounted for by any other demonstrable process, warrants the diagnosis, and the demonstration of the pneumococci and the pneumococci only in the blood warrants the reference of the endocarditis to that organism.

Case II.—A girl, aged eighteen years, entered with the following history: Fourteen days before entrance she had a severe chill, lasting two or three hours, followed by rise of temperature, pain in the left side, and cough. After the chill, severe pain in both feet and later in knees, wrists, and elbows, lasting altogether for nearly a week. At entrance the girl had a temperature of 103.2°; pulse, 120, and respirations 42. Physical examination showed a pneumonia of both lower lobes. Painful swelling of the left hand. Heart was negative. The urine negative. Leukocytosis of 12,600. Pneumococci in the sputum. The case ran a very severe and protracted course. The maximum temperature was 106.2°, the pulse 160, and the respirations 64. It was fully expected that the girl would die, but gradually, after three weeks in the hospital—*i. e.*, at the end of the fifth week—the temperature had returned practically to normal, the pulse and respirations had slowed, and resolution was progressing. This satisfactory condition continued for five days, when the temperature began again to go up, and within twenty-four hours had reached 103.6°, with pulse of 156, and respirations of 32. Numerous joints became painful. Three days later systolic and diastolic murmurs appeared over the apex. The blood showed a moderate leukocytosis, and so many pneumococci that they could be found in every blood smear easily. Pure cultures were obtained.

The temperature remained continuously high for six days, and then returned to normal, and remained there during the long period of her convalescence. The girl left the hospital ninety-six days after entrance restored to health, but with a well-characterized double lesion of the mitral valve and orifice.

This case is striking in many ways, but particularly in that the diagnosis of pneumococcus endocarditis seems as well grounded as any clinical diagnosis can be, and yet the patient recovered. So far as I know it is the only one on record, except the case reported by Dr. Edward Wells, of Chicago, and one by Robison, of Chicago, in which cases, however, there was no demonstration of the pneumococci in the blood.

Case III.—A male, aged thirty-five years, entered about the fourth day with a pneumonia of the right lower lobe. The previous history could not be obtained, because the pulmonary condition was complicated by a serious alcoholic delirium. The temperature at entrance was 100.6°, pulse 120, and respirations 40. The heart was negative. Leukocytosis of 10,000. Pneumococci in the sputum. Urine negative. The man was seriously ill, but presented no unusual phenomenon, and the fifth day after entrance had a normal temperature, pulse, and respiration, and was apparently convalescent. This condition persisted for three and one-half days, when he had a very hard chill, and the temperature rose to 103.2°. The physical examination was negative, but three days later a systolic murmur appeared over the apex, and persisted with gradually increasing intensity to the death. The temperature ran a very irregular course, often reaching 104° or 105°, and irregularly interrupted by severe chills. The number of leukocytes fell to 6750, and although the blood was examined repeatedly for pneumococci, none were found until the thirty-second day of his illness. During the night of the thirty-first day numerous small hemorrhages appeared in the skin, particularly of the neck and thorax, but to some extent also over the limbs. Blood cultures taken the morning after the appearance of the eruptions yielded a pure culture of the pneumococci. The condition of the patient through all these days was gradually getting worse and worse, and he died during the thirty-eighth day after entrance, and the forty-second of his illness.

The clinical diagnosis was an acute endocarditis of the mitral valve, due to the pneumococcus. Fortunately, it was possible to obtain an autopsy, with the following findings: The lungs had practically returned to their normal state, although the right lower lobe, the site of the pneumonia, was somewhat firmer than the other lobe. The pleural and pericardial cavities were normal. The heart was normal in size, but showed three or four small subpericardial hemorrhages, particularly over the wall of the left ventricle. All of the valves were normal, except the mitral, which showed a polypoid, dirty, greenish-colored, irregularly granular,

firm vegetation about the size of a hazelnut. The base of this vegetation was about ½ cm. in diameter. Along the line of closure of the other portion of the mitral leaflets were small, pinhead-sized, warty vegetations. The spleen showed a single large infarct. Both kidneys were the site of infarcts, and dissection of one of the infarcts showed the embolus plugging the vessel. Smears from the vegetations taken at once showed only the pneumococci present in large numbers. The cultures, which could not be taken for some hours, were contaminated with some form of saprophytic bacilli. The cultures gave the pneumococci plus these bacilli. A rabbit inoculated through the veins of the ear with this mixture died within twenty-four hours of a lobar pneumonia, from which pure cultures of the pneumococci were obtained.

The cerebrospinal axis was not examined, but there was no reason clinically to suspect a complicating meningitis.

In 1885 Netter published a very careful and exhaustive review of this subject, covering 82 cases. Since that time 50 cases have been added, and a review of the entire 132 might be profitable.

The frequency with which pneumonia is complicated by endocarditis cannot be positively stated, because there is no reason to doubt that a certain percentage of the cases of endocarditis pass unrecognized clinically, until they later appear suffering from the effects of a chronic endocarditis. Aufrecht says that he found but a single instance of endocarditis in 1501 personal cases of pneumonia—*i. e.*, 0.06 per cent. Fismer found it twice in 230 cases—*i. e.*, 0.9 per cent. of his cases. Wells, in 6050 collected cases of pneumonia, found 19 of endocarditis—*i. e.*, 0.3 per cent., and in 1213 fatal cases there were 47 cases of endocarditis—*i. e.*, 4 per cent.

Kerr, in a review of 171 cases of pneumonia upon the autopsy table at the Cook County Hospital, found 14 instances of endocarditis—*i. e.*, 8.2 per cent. Osler reports 16 cases of endocarditis in 100 fatal pneumonias. Sears and Larrabee found 9 cases of endocarditis in 291 deaths from pneumonia—*i. e.*, 3.1 per cent. Omerod, in 183 cases of pneumonia and pleurisy, found 6 of endocarditis—*i. e.*, 3.3 per cent. Norris, in 500 cases of pneumonia from the Pennsylvania Hospital, found 5 cases of endocarditis—*i. e.*, 1 per cent. Liebermeister found endocarditis but once in 254 cases treated in the Tübingen Clinic—*i. e.*, 0.4 per cent. Sello found only 6 cases in 750—*i. e.*, 0.8 per cent. Adding these figures we get 11,243 cases of pneumonia, with 126 cases of endocarditis—a percentage of 1.1. If we take out the reports based upon the autopsy records, we find 1775 cases, with 86 instances of endocarditis—a percentage of 4.28. The percentage given by various authors ranges from the maximum of 16 per cent. in 100 fatal cases to a minimum of 0.06 per cent. by Aufrecht, from 1501 personal observations, of which 253 died; but it is probable that the average is about 1 per cent. of all cases, and 5 per cent. of the fatal cases.

What is the frequency of pneumococcus endocarditis as compared with other forms? Wells collected 517 cases of fatal endocarditis, 115, *i. e.*, 22.3 per cent., of which were in connection with pneumonia.

Lenhartz found pneumococci in 9 of 28 cases of endocarditis—*i. e.*, 32 per cent. Kerchensteiner found 6 in 23 cases of malignant endocarditis—*i. e.*, 26 per cent. Osler found pneumonic endocarditis in 25 per cent. of the cases. Kauthach and Tickell found it in 14 per cent. of 84 cases. Harbitz, in 43 cases of infectious endocarditis, found 5 due to the pneumococcus—*i. e.*, 11.6 per cent. Weichselbaum found the pneumococci in 7 of 33 cases—*i. e.*, 21.5 per cent. Totalled, these make 944 cases, with 208 associated with pneumonia—*i. e.*, 22 per cent. Taking the 127 cases of malignant endocarditis studied bacteriologically by Lenhartz, Kerchensteiner, Harbitz, and Weichselbaum, we find 27 due to the pneumococcus—*i. e.*, 21.2 per cent. Only the streptococci and staphylococci are found more often than the pneumococci in the fatal endocarditis, and they are only a little more frequent.

The relative frequency of the verrucose and ulcerative endocarditis is not to-day a matter of great importance, for we now realize that the two forms differ in degree only, and not at all in kind. In a general way, however, it is true that the greater the exudate upon the valves the greater the seriousness of the case, and while the pneumococcus may cause either small or large vegetations upon the valves, they are generally large. In some cases both large and small vegetations are found in the same case. Case II. of the personal cases reported above will serve as an illustration of this. Of 39 cases published since the article of Netter, in which the character of the endocardial exudate is mentioned, 30 are described as large, polypoid, cauliflower-like, ulcerative; 7 are described as small and warty, and in 2 cases both forms of exudate occur. Of the 14 cases in Kerr's report, 12 are described as ulcerative, and 2 as vegetative. Osler, in 16 cases, found 5 verrucose and 11 ulcerative. Norris describes 4 out of his 5 cases as malignant. These cases would place the severer forms of endocarditis at 77 per cent., the milder at 20 per cent., and both together at 3 per cent. In other words, if an endocarditis develops in the course of a pneumonia, it is four to one that it will be of the so-called ulcerative or malignant type.

The descriptions of the valvular exudate given by the various authors correspond closely. The exudate is often large, described as the size of a pea, a bean, a walnut, and up to an inch and a half in length. Cauliflower-like is a word frequently employed in the description, and is appropriate to a considerable number of the cases. The mass is firm and granular, reddish-gray, yellow to green in color. Polypoid is another word constantly recurring in the reports. Aneurysm and perforation of the valves is less com-

mon in cases due to the pneumococcus than in those due to the staphylococcus and streptococcus. Kerchensteiner regards the following features as characteristic of pneumococcus vegetations: 1. Midway between ulcerative and verrucose form. 2. Large vegetations, with wide base. 3. Smooth, discolored surface. 4. Tendency toward softening. I do not, however, place any confidence in this effort at characterization of the pneumococcus vegetations, for just as the pneumococcus may produce vegetations ranging from the smallest to the largest, so, also may any of the numerous bacteria now known to be capable of exciting endocarditis. The only way in which one can determine the bacteria exciting the endocarditis is by examination of the exudate.

While the inference always is that an endocarditis occurring with a pneumonia is due to the pneumococcus, a few exceptions have been recorded. Thus Jaccoud, in his clinical lectures of 1885 and 1886, reports a case of pneumonia complicated by endocarditis in which a streptococcus was the cause. There are reports of 69 cases, which include a bacteriological examination. In but 9 of these is there any report of the ante-mortem examination of the blood for bacteria, and 3 of these are the personal cases reported above. In 1 other case, that of Dr. Wells, the blood was examined for this purpose, but with negative results. The reason for this is that the bulk of the reports antedate the introduction of the modern methods of taking blood cultures, which are modifying our ideas on so many subjects.

In 64 cases only the pneumococcus was found—three times in connection with the streptococcus, once streptococcus only, and once streptococcus and staphylococcus. Something over 94 per cent. of the cases of endocarditis complicating pneumonia are due to the action of the pneumococcus.

There are reports covering 141 cases,[1] in which the valves affected are stated. In 116 of these the endocarditis is confined to the left side of the heart, in 17 to the right heart, and in 8 both sides are affected. Put into percentages, the figures are 82.2 per cent. left, 12 per cent. right, and 5.7 per cent. bilateral. A comparison of these percentages with those derived from the 2435 of valvular lesions tabulated by Jürgensen, in his article upon endocarditis in the Nothnagel *System*, is interesting. These percentages are 94.3 per cent. left heart, 2.7 per cent. right heart, and 2.8 per cent. bilateral.

To put it in another way: In 17.8 per cent. of the cases of pneumococcus endocarditis the right heart is affected, while only 6.7 per cent. of cases of endocarditis in general are right-sided.

[1] The number of cases, as stated earlier in the article, 132, includes only those given with clinical details. There are nine other cases, in which only the valve affected and the relation to pneumonia is stated.

The distribution among the valves is shown in the following table:

Aortic only	56	39 7 per ct.
Mitral only	40	28.3 "
Aortic and mitral	20	14.1 "
Tricuspid only	12	8.5 "
Pulmonary only	5	3.5 "
Aortic, mitral, and tricuspid	5	3.5 "
Mitral and tricuspid	2	1.4 "
Aortic and tricuspid	1	0.7 "
	141	

Comparing these percentages with those derived from Jürgensen's table, we have:

Aortic only	39.7 per ct.	18.7 per ct.
Mitral only	28.3 "	66.3 "
Aortic and mitral	14.1 "	9.2 "
Tricuspid only	8.5 "	0.4 "
Pulmonary only	3.5 "	2.3 "
Aortic, mitral, and tricuspid	3.5 "	1.0 "
Mitral and tricuspid	1.4 "	1.8 "

The striking things about this table are that the pneumococcus is something over twice as apt to involve the aortic valves as the other bacteria, and about one-third as apt to involve the mitral, while it attacks the tricuspid valve twenty times as often.

Another question bearing upon the site and character of the exudate is that of infarcts. It has been repeatedly stated that infarcts are exceptional in this class of cases, but in 20 of the 50 cases added to those of Netter infarcts were found in spleen, kidney, lungs, brain, or intestine; six in the spleen only, twice in kidney only, seven in spleen and kidney both, four times in the lungs, and twice in the brain. From this we must say that infarcts do occur with this form of endocarditis.

In 1862 Heschl drew attention by a report of 5 cases to the frequency with which endocarditis complicating pneumonia is found in association with meningitis. Netter fully confirmed this statement, for he found the coincidence of these two complications in no less than 45 of 63 cases, in which the records were sufficiently full to supply information upon this point. This amounts to 71.4 per cent. Of the 50 cases since Netter's paper, 19 had a meningitis, a rather smaller percentage, and together the percentage is 56.6 per cent.

Meningitis is a much commoner complication of pneumonia than endocarditis, and while approximately 60 per cent. of the cases of endocarditis are associated with meningitis, only about 30 per cent. of the cases of the latter are accompanied by the former.

What are the factors which favor the development of a complicating endocarditis?

Of 132 cases, 92 are males and 40 females—*i. e.*, 69 per cent. and 31 per cent.

It is generally stated that pneumonia is from three and one-half to four times as common in males as in females, and the figures quoted place endocarditis in males at approximately twice as common as in the females. It would seem, therefore, that the female is about twice as prone to endocarditis as the males.

A consideration of the age of the patients brings out some interesting facts. The following table shows the percentage of cases of endocarditis, distributed according to decades, and in comparison with them the age distribution of cases of pneumonia as derived from Aufrecht's article:

	Pneumococcus endocarditis.		Pneumonia.
1st decade	2	1.4 per ct.	6.8 per ct.
2d decade	8	5.7 "	22.2 "
3d decade	15	10.8 "	29.0 "
4th decade	42	30.4 "	17.0 "
5th decade	27	19.5 "	13.0 "
6th decade	29	21.0 "	5.5 "
7th decade and over	15	10.8 "	6.0 "

This shows that while 58 per cent. of all cases of pneumonia occur during the first three decades only, 17.9 of the cases of pneumococcus endocarditis occur during the same period; that the fourth, fifth, and sixth decades supply 35.5 per cent. of the pneumonias and 70.9 per cent. of the endocarditis. This is in marked contrast to other infectious diseases, which are prone to involve the endocardium. The rheumatism, for example, causing endocarditis in a large percentage of even mild cases under twenty, while it rather infrequently involved the endocardium in the adult.

The influence of an antecedent endocarditis is considerable. Thus, of the 50 cases added in this article, 12—approximately 25 per cent.—showed old endocarditis upon which fresh vegetations had developed. Sears and Larrabee state that of the 945 cases reviewed by them, 80 had chronic endocarditis; that 4 of these went to the autopsy table, and 3 of them showed a fresh endocarditis.

Other factors which may be considered as having a predisposing influence toward the development of endocarditis are alcoholism, anæmia, debility, or malnutrition from any cause. The character of the epidemic seems to have some influence upon this, as upon other complications; for example, Netter knew of 7 cases in the various hospitals of Paris during the year 1885. Pathological specimens from 3 cases were shown before the Chicago Medical Society during the current year.

The manner in which the pneumococci become implanted upon an intact endocardium is as obscure as the reason why they prefer the aortic to the mitral valves. The experimental production of endocarditis by inoculation with the pneumococcus is usually unsuccessful, unless the valves are previously injured by the method of Orth and Wyssokowitsch, but occasionally endocarditis results without any antecedent injury. Michaelis, in 1895, showed the

heart of a dog which died in the course of immunization to the pneumococcus from an acute endocarditis of the aortic and mitral valves. The pneumococci were demonstrated in the vegetations.

It has been suggested that the endothelial cells, which possess the power of protruding pseudopodia and are also phagocytic take up the bacteria from the blood. If the bacteria are thus destroyed well and good, but if, on the other hand, the endothelial cells are destroyed the surface of the valve is roughened, fibrin cells and more bacteria are deposited, and endocarditis results.

One might infer that the pneumococci in these cases are particularly virulent, but upon this point we have very little information. Fraenkel reports a case of malignant endocarditis due to the pneumococcus lasting six months. The cocci were repeatedly obtained by blood cultures, but were of such reduced virulence that they did not cause fatal septicæmia in animals.

Turning, now, to the clinical aspect of this condition, it becomes necessary to divide the cases into two groups: those which are latent—*i. e.*, do not cause any symptoms which permit of their clinical recognition—and, secondly, those in which the clinical diagnosis is possible.

The first group is and must remain the larger. When the endocarditis develops during the height of a pneumonia the constitutional symptoms would be lost in those of the primary localization of the pneumococcus, and the physical signs from the heart require time for their development, so that death occurs before there is data upon which to base the clinical diagnosis. The possibility of an endocarditis should be kept in mind, particularly with patients beyond thirty years of age, and of the female sex. Frequently repeated and careful examinations of the heart will detect an endocarditis which must otherwise be overlooked. One must not, however, be too ready with the diagnosis. With pneumonia, as with the other infectious fevers, systolic murmurs frequently appear without there being an endocarditis. Systolic murmurs without any supporting evidence should be looked upon as accidental. Diastolic murmurs here, as elsewhere, have a high significance, and, appearing in the course of a pneumonia, must be referred to an endocarditis.

The symptoms resulting from pneumococcus endocarditis do not present any marked difference from those resulting from endocarditis from other bacteria. Temperature is present in practically every case, although in rare instances there is no temperature. Lesage and Pineau report a case of three months' duration without there being at any time any elevation of temperature. The temperature is usually very irregular, interrupted by chills, repeated at irregular intervals, and rising frequently to 104° or 105°. Exceptions sometimes occur, and show a continuous or regularly intermittent fever. The temperature of the pneumonia may pass without

interruption into that of the endocarditis, but in a very considerable proportion of the cases there is a period of a few days of freedom from fever intervening.

Netter was familiar with this afebrile period, but gives no accurate data. Of 20 cases in which there is an afebrile period, it is found to vary from a portion of one day up to twelve and more. In 4 of these cases this period is said to have been several days, without specifying the number; 13 of the other 16 had a period of seven days or less, and 10 of these 13 showed a period of four days or less.

The duration of the temperature varies over wide limits, from a few days to weeks or months. Inasmuch as it is never possible to fix the exact date of the onset of the endocarditis, the figures here given are for the entire duration of the illness. This is given in 109 of the reported cases, and ranges from a minimum of seven days to a maximum of one hundred and eighty days, and averages thirty days.

As a general proposition, those cases in which a meningitis develops are shorter than the others, but even with this complication they may last for weeks.

The pulse rate in the cases varies so greatly that it is as impossible to make any general statement in regard to it as it is in regard to the course of the temperature. The pulse rate may follow the course of the temperature, and be proportionate to it, but in other cases it is far more rapid than the temperature would lead one to expect, while in other cases there is a marked bradycardia. The bradycardia in some cases is the result of a complicating meningitis, but is also seen in cases which do not present any manifestations of the latter.

The pulse rate is greatly influenced by movement, a change in position causing an abnormal amount of change in the rate of the heart's action. There is often also marked change in the pulse count from minute to minute.

So far as subjective symptoms referable to the heart are concerned, they are the exception rather than the rule, and when they are prominent are practically always the result of an old heart lesion. Palpitation, oppression, and pain may occur.

Physical signs are entirely lacking in many of the cases. Here, as with other forms of endocarditis, the auscultatory signs appear before the percussorial. The site and time of the resultant murmur or murmurs are of course determined by the site of the endocarditis. If the murmur is purely systolic one must be cautious about its interpretation. A well-localized systolic murmur, which persists and which gradually increases in intensity, must be looked upon with anxiety, if there are constitutional symptoms not sufficiently accounted for by a process elsewhere in the body; but, again, we must urge a caution against mistaking the often loud systolic murmur, found over the hearts of people who are or have been seriously ill, for one due to actual endocardial changes.

If diastolic murmurs appear, they may be safely referred to an endocarditis.

In a certain proportion of the cases a pericarditis develops, and it may be impossible to determine clinically whether the murmurs heard are endocardial or pericardial.

Changes in the size and shape of the area of cardiac dulness are found in a certain small proportion of the cases, even in those in which the endocarditis is purely acute.

Alteration in the rate and rhythm of the respirations is due rather to the changes in the lungs and pleuræ than to those in the heart, but the possibility of pulmonary infarction must be kept in mind in the cases in which the right heart is involved. The symptoms of such infarction are determined largely by the size of the infarct, and vary from nothing at all to severe and sudden dyspnœa and hæmoptysis.

Urinary changes are those common to infectious processes; concentrated and high-colored urine, in which albumin and casts are often found. If infarcts are formed in the kidney—and this, as has been pointed out, occurs rather frequently—the kidney may become painful and blood appear in the urine. In many cases no clinical symptoms result, or are overlooked in the multitude of other and more striking features.

The spleen is often enlarged, the tumor being a part of the picture of a severe infection. It also is a frequent site of infarction, which may show itself by pain and sudden increase in the size of the spleen. A localized peritonitis often results, and may cause audible and palpable friction. The liver in some cases is swollen from passive congestion, and jaundice may occur. The exact etiology of such jaundice is as obscure here as in other severe acute infections.

A small percentage of the cases show changes in the skin in the way of localized erythema, or more often in the shape of purpura. Herpes, particularly over the distribution of the middle and lower branches of the fifth cranial nerve, is common here, as in other instances of infection with the pneumococcus.

Arthritis is a rather frequent complication of these cases, and while this has been proven to be due to the pneumococcus, in but few instances, it is highly probable that the organism could be demonstrated in the bulk of these cases.

Last, and in some ways the most important, are the blood changes. Leukocytosis is the rule in pneumococcus infections, but, exceptionally, and this is particularly true in very severe cases, among which we must place those in which endocarditis has occurred, the white blood corpuscles are often not at all increased in number; may be even reduced. The red blood cells and the hæmoglobin are reduced. More important still is the fact that the pneumococcus can be demonstrated by culture or by smear from the circulating blood. The number of cases in which this has been so far

done is still small, only 9 in number, but in view of the fact that the pneumococci are found in the blood in something over 80 per cent. of all cases of pneumonia, we must believe that they would be found equally often in this class of cases, if sought for in the proper manner. Repeated examination may be required, as is illustrated by the third of the personal cases reported, in which repeated effort failed to find them until after the appearance of the purpura, when they were very readily found.

The diagnosis of an endocarditis must rest upon physical signs, which should be faithfully looked for in all cases of pneumonia, and particularly in a case which does not end at the proper time, but runs over into a high and irregular temperature, with repeated chills. If such a temperature is not accounted for by a delayed resolution, an empyema or some other demonstrable complication, the possibility, even probability, of a complicating endocarditis must be seriously in mind, even though the physical examination of the heart shows nothing.

Before leaving this question it should be stated that the pneumococcus can excite an endocarditis without there being any involvement of the lungs at any time. In such cases the clinical diagnosis may not be carried beyond the point of diagnosing an acute endocarditis, unless the bacteriological examination of the blood shows the pneumococci.

The prognosis is shown by the fact that in the 132 cases there are but 4 recoveries, and in but 1 of these is the diagnosis complete—*i. e.*, an endocarditis is observed at the time the pneumococci are circulating in the blood. I am not, however, of the opinion that this represents the true mortality rate, for I cannot but believe that there are cases of pneumonia which recover even though there is a complicating endocarditis.

No one who has ever seen the heart from a case of this sort has much to say in regard to the treatment, for its futility is too obvious. If the vegetations are small, the virulence of the bacteria low, the resistance of the individual high, the patient may recover, but these factors cannot be estimated in the present state of our knowledge, and only the last one can be influenced.

Proper food; absolute quiet, physical and mental; stimulant medication, the reduction of temperature by hydrotherapy, and the use of the ice-bag over the heart practically exhaust our therapeutic means. Various drugs, such as the salicylates, the oil of wintergreen, the creosote derivatives, silver salts, and others are employed, but, it must be admitted, without demonstrable effects.

Conclusions. 1. Endocarditis complicates pneumonia in about 1 per cent. of all cases, and in 5 per cent. of the fatal cases.

2. Endocarditis due to the pneumococcus makes about 25 per cent. of all cases of bacterial endocarditis.

3. The pneumococcus may cause endocarditis of any degree of

intensity, but in over three-fourths of the cases it is of the severe or so-called malignant type.

4. The exudate is usually massive, but there is less disposition to ulceration and perforation of the valves than in endocarditis due to the streptococci and staphylococci.

5. The endocarditis complicating pneumonia is almost always due to the pneumococcus, although it may be due to other bacteria.

6. Pneumococcus endocarditis is much more often left than right-sided, but involvement of the tricuspid and pulmonary valves occurs about four times as often as it does with endocarditis in general.

7. The pneumococcus attacks the aortic valves more often than the mitral, and relatively twice as often as the other organisms commonly causing endocarditis.

8. The pneumococcus attacks the mitral valve relatively only half as often as other organisms, while it attacks the tricuspid about twenty times as often.

9. Infarcts occur in about one-half the cases.

10. Meningitis complicates the pneumococcus endocarditis in about 60 per cent. of the cases.

11. Pneumococcus endocarditis is relatively twice as common in females as in males.

12. Endocarditis complicates pneumonia much more frequently after thirty years of age than before.

13. An old heart lesion favors the development of pneumococcus endocarditis.

14. The clinical picture of pneumococcus endocarditis does not differ from that due to any acute endocarditis.

15. The endocarditis may develop before, during, or after the pulmonary involvement, but the pneumococci may infect the endocardium without there being at any time any involvement of the lungs.

16. A considerable number of the cases show a period of normal temperature between the fever due to the pneumonia and that due to the endocarditis.

17. This afebrile period is rarely longer than a week, and is usually only three or four days.

18. The endocarditis may be afebrile.

19. The duration varies from a few days up to months.

20. The pulse is usually rapid and irritable, but bradycardia is more frequent than in other forms of acute endocarditis.

21. Subjective symptoms referable to the heart are usually absent, except in cases where there is an old heart lesion, when they are due to the old rather than the fresh endocarditis.

22. Physical signs of the endocarditis are often entirely lacking.

23. Signs and symptoms from other organs are either those common to infectious processes or are due to infarcts, in which case they vary with the size and site of the infarct.

24. Leukocytosis is frequently absent.

25. Blood culture, carefully and perhaps frequently repeated, will show the pneumococci.

26. The diagnosis is difficult, impossible, in fact, in cases in which the endocarditis develops during the course of the pneumonia, and ends rapidly in death.

27. Endocarditis should always be suspected in a case of pneumonia which is followed by an irregular temperature not sufficiently accounted for by some other complication, such as empyema.

28. Case II. of the personal cases is the only one so far recorded ending in recovery, admitting for the sake of argument that Case I. is really not what it was supposed to be. The cases of Wells and Robison lack the demonstration of the pneumococci in the blood.

29. The prognosis is extremely grave, for 60 per cent. of the cases have a complicating meningitis, but it is probable that the percentage of recovery is higher than the reports so far published would lead one to infer.

30. The treatment consists merely in rest, absolute rest, with good, supporting food, and stimulation as required.

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A CONTRIBUTION TO THE STUDY OF ULCERATIVE ENDOCARDITIS.

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It is the writer's intention in this article to give a short *résumé* of the history of ulcerative endocarditis, the pathological anatomy of the disease, and the etiological factors, together with a short synopsis of thirty-two cases.

In the recapitulation the writer takes up the varieties of the disease, with the principal symptoms as found in his collection.

The names of Bouillard and Stenhouse Kirkes are prominent among those who first recognized that there is a form of endocarditis more malignant in its course and termination than the simple acute variety.

Virchow first showed the embolic nature of the plugs occurring in the arteries.

Winge was the first, however, to describe microbes found on the valves and in the metastatic infarcts; these he described as chains of small rods or of small round granules.

Heilberg also found organisms of a similar character in a case of endocarditis in a puerperal state; he excised particles of the valves and injected them into rabbits, but without effect. Numerous inoculation experiments followed, and Birch-Hirschfeld succeeded in

causing panophthalmitis in three rabbits by inoculation with fragments of valve deposits.

From 1885 to 1888 numerous interesting observations were published, most important of them being those of Netter, Weichselbaum, Orth, Wyssokowitsch, and Rosenbach. The investigations showed that by injecting into the external jugular vein pyogenic organisms, as streptococcus pyogenes, staphylococcus pyogenes aureus, and others, an artificial endocarditis could be produced. The experiments were more apt to be successful if the valves or arterial surfaces were injured before the introduction of the germs; the injury being caused by a sterilized stylet passed through the carotid artery into the left ventricle (Rosenbach). However, Dreschfeld has succeeded in producing the disease without previously wounding the valves. The resulting organisms were found on the valve surface and in the metastatic emboli.

Most recent investigators are of the opinion that the difference between *simple acute* and *ulcerative* endocarditis is one of degree, depending upon the virulence of the invading organisms or their toxins, or susceptibility on the part of the patient. Bacteria are found in the valves of both forms; almost *always* in the ulcerative variety, *often* in the simple form, and the same organisms are found in both. According to Weichselbaum, "acute endocarditis chiefly affects the valves, especially of the left heart, and appears to be practically always due to bacteria; the micro-organisms affect the valves either primarily or are derived from other organs. An anatomical distinction between ulcerative and verrucose forms can be drawn only according to the *destructive* character of the inflammation. The difference is entirely one of degree, dependent upon the quantity and the virulence of the bacteria. In the *ulcerative* variety the *necrotic destruction and the surrounding inflammation* is much more extensive than in the other, and leads to the formation of ulcers, erosion, miliary aneurysms, and perforation of the valves." Dawson Williams thinks that when the right heart is attacked it is by secondary infection.

Harbitz records 39 cases which he considers of the infectious type. In 6 cases the ulcerations had healed and presented outgrowths on the endocardium; at the edges of the vegetations masses of bacteria were aggregated, but cultures remained sterile. He makes two classifications pathologically—one with vegetations and excrescences on the endocardium, the other with destruction of tissue ulceration. Osler says that in 75 per cent. of cases the infectious form is engrafted upon a previous endocarditis. In his collection of 209 cases the tricuspid valve was involved alone in 19, the pulmonary in 15, aortic alone in 55, mitral alone in 17, aortic and mitral together in 41, heart walls in 33, and the right heart alone in 9.

Jackson reports 59 cases, with autopsies in 43. The mitral valve alone was affected in 15, the aortic in 9, both together in 10, and

the right heart showed lesions in 6 cases. Small abscesses of the brain and purulent meningitis were often seen, and organisms resembling cocci morphologically were frequently found in sections of the endocardium.

In 44 cases of the ulcerative type reported by Thayer and Lazear the right heart was affected in 15.91 per cent.

Out of 802 *benign* cases in the Münich statistics the right heart alone was affected in 3.25 per cent.[1]

The *organisms* most frequently found are the streptococcus pyogenes, staphylococcus pyogenes albus and aureus, pneumococcus of Fraenkel, or diplococcus lanceolatus; less frequently the gonococcus, typhoid bacillus, bacillus of tuberculosis, bacillus of diphtheria, and the colon bacillus. Streptococcus pyogenes and staphylococcus pyogenes aureus are found in cases in which the endocarditis is apparently primary; in septic and pyæmic conditions, as wounds, abscesses, the puerperal state, erysipelas, etc.; in cases where there is a pre-existing valvular lesion, due to previous rheumatic disease. These two organisms have also been found upon the valves in cases complicating typhoid fever, gonorrhœa, diphtheria, etc., as showing a type of mixed infection. The diplococcus lanceolatus has been found mostly where croupous pneumonia or meningitis has been present, although two cases are cited in this series where neither lesion existed, but a previous endocarditis had occurred.

Blood cultures were taken in 23 of Jackson's 59 cases; streptococcus was found in 8, micrococcus lanceolatus in 5, staphylococcus in 3, colon in 1, streptococcus and staphylococcus together in 1, and streptococcus with unknown organisms in 1.

Of the writer's cases staphylococcus was found in 4, micrococcus lanceolatus in 3, staphylococcus and pneumococcus together in 1, streptococcus in 2 cases.

According to Dreschfeld "the following types of malignant endocarditis are recognized: (*a*) primary; (*b*) as a complication of septic diseases; (*c*) as a complication of pneumonia and meningitis; (*d*) as a mixed infection secondary to the acute infectious fevers, to rheumatic endocarditis, or to a sclerosis of the valves."

The primary cases are admittedly rare. Pneumonia is a frequent cause, as is meningitis, also septicæmia from whatever origin; rheumatic fever, and less frequently typhoid fever, influenza, diphtheria, scarlet fever, tuberculosis, variola, and measles,.

Of the writer's 32 cases 8 occurred coincidently with rheumatism, 1 apparently with a strain of the back accompanied by hæmaturia, 7 gave a history of old rheumatic attacks, 3 of having had scarlet fever or diphtheria. 2 of palpitation and dyspnœa, 7 of typhoid

[1] In looking up the records of cases of *simple* mitral stenosis the writer has collected 50 cases, in which 12 (24 per cent.) showed lesions of the tricuspid valve. These give the largest percentage of right heart inflammation he has yet seen (report of the Cornell University Dispensary, 1904).

fever, influenza, or malaria, the remainder having apparently always been well.

The disease is rare among young children. Osler gives but 3 cases in his collection of 109. The records of the Children's Hospital at Melbourne furnish but 1 case in ten years. Davies finds but 1 case in the *Transactions of the Pathological Society* (London). Only 1 case appears in the records of the London Hospital for Sick Children from 1870 to 1890, and S. S. Adams reports but 1 case in the Children's Hospital, Washington, D. C., since 1870.

S. S. Adams has collected all the cases reported in children under fifteen years of age—46 in all—3 congenital, 1 of eight months, 1 of ten months, 1 of eleven months, 3 of three years, 2 of four years, 3 of five and a half years, 2 of six years, and the others of seven and over. The diseases preceding or accompanying this condition were: maternal erysipelas and fetal infection (cultures from the cord showed streptococci); malaria, 1 (æstivo-autumnal); acute miliary tuberculosis, 1; vaginitis, 1; remitting fever, 1; rheumatism, 3; chorea, 2; rheumatism and chorea, 1; typhoid fever, 2; empyema, 1; trauma, 1; otitis media, 1; old cardiac disease, 5; caseous tubercle, 1; diphtheria, 1; influenza, 2; erysipelas, 1; tonsillitis, 1. The rest are not given.

Of the 46 cases, the heart wall was affected in 6, the tricuspid valve in 5, the pulmonary valve in 2; one had a patent foramen ovale, and in the others the left heart was the seat of inflammation.

No cases have occurred in young children in the Presbyterian Hospital during the last ten years.

Group I.

The following collection of cases is one in which the staphylococcus pyogenes aureus was found. The albus, which was obtained in a number of cases, is considered only as a skin contamination.

Case I.—Aged thirty-seven years, male, attendant, admitted February 3, 1900; died February 9, 1900. Two of the family died of pulmonary tuberculosis. The patient drank moderately, but never had syphilis or rheumatism.

The present illness began one week before admission with the sudden vomiting of about a pint of blood, followed by a pain over both hypochondriac regions. Three days later he had retention of urine.

The *physical examination* upon admission showed nothing, but the following day the temperature began to rise irregularly, reaching 107° on the third day, continuing on the fourth day, and then falling slowly to 103°. During this time he developed a pericardial friction sound. The second day he had three convulsions, with great increase in arterial tension. Examination of the urine showed 15 per cent. of albumin (by volume), hyaline and granular casts,

and red blood cells. Symptoms of meningitis soon followed, with headache, violent delirium, retraction of the head, rigidity of the muscles of the neck, back, and extremities, and general hyperæsthesia. Blood culture proved a pure growth of staphylococcus pyogenes aureus. There were no petechial hemorrhages, no chills; there was no splenic enlargement, nor any reaction to Widal test.

Upon *autopsy* the heart weighed nine and one-half ounces; the pericardium was normal, but the mitral valve showed small, white, soft, vegetations; the spleen and the kidneys were apparently normal.

Cultures from the spleen and brain showed staphylococcus pyogenes aureus.

Case II.—Aged twenty-five years, housewife; admitted May 7, 1899; died May 9, 1899.

There was no family or previous history of note, with the exception of an attack of rheumatism fourteen months before admission. Dating from this, however, the patient had attacks of cardiac palpitation and dyspnœa.

The present illness began five days before admission, with sudden vomiting, dizziness, and high fever, preceded by dull pain in the joints. Two days after this a bright-red eruption occurred on her feet and legs, accompanied by severe epistaxis.

The *physical examination* showed evidence of mitral insufficiency; the presence of a rather profuse hemorrhagic eruption, and marked delirium. The temperature was 106°, pulse 120. After admission the temperature continued high. The blood showed 19,000 leukocytes per c.mm. Culture gave an abundant growth of staphylococcus pyogenes aureus. There were no chills, no splenic enlargement, and no reaction to Widal test. Autopsy could not be obtained.

Case III.—Aged eighteen years, housewife; admitted February 17, 1902; died February 21, 1902.

The patient was a premature child, and while young had scarlet fever, diphtheria, acute articular rheumatism, and typhoid fever. She had frequent attacks of cardiac palpitation and dyspnœa, and during her pregnancies was uræmic; she was not alcoholic, but was a confirmed tea drinker. For eleven weeks previous to admission she was short of breath, had dyspnœa and palpitation, nausea, occasional vomiting, and diarrhœa.

Examination revealed a dilated heart, in which evidence of mitral and tricuspid incompetency existed; there was subcutaneous œdema, and dropsy of the serous cavities. The liver and spleen were both palpable. The course of the temperature was from 103° to 104°, and continuous. The blood examination revealed 37,000 leukocytes to the cubic millimeter, and the presence of staphylococcus pyogenes aureus; there was no reaction to Widal test. The urine contained a trace of albumin and much blood. There were no subcutaneous hemorrhages.

Case IV.—Aged thirty-six years, male, butcher; admitted October 31, 1901; died November 14, 1901.

Family history was unimportant. The patient had rheumatism of the subacute variety at twenty-five years of age, and gonorrhœa four years ago. For four months before admission he felt languid and listless, with dyspnœa, dry cough, precordial pain; at two different periods he had profuse hemorrhagic eruptions.

Upon *physical examination* mitral, systolic, and aortic diastolic murmurs were heard; the heart was enlarged, and compensation had broken. The liver could be felt three inches below the costal margin. The spleen was enlarged. After admission petechial hemorrhages developed. The temperature was irregular and not higher than 101°, the pulse 168. Leukocytes, 27,000 per c.mm.; hæmoglobin, 85 per cent. A growth of staphylococcus pyogenes aureus was obtained upon culture. No autopsy was granted.

Group II.

The following cases constitute a group in which the infection is by the micrococcus lanceolatus. The first two cases were reported by Dr. Walter B. James in the *Presbyterian Hospital Report* of 1898, and are here entered through his courtesy. It is of interest to note that none of them were accompanied by pulmonary complications.

Case V.—Aged nineteen years, German; admitted May 1, 1887; died May 28, 1887.

There was no family or previous history of note. The present trouble began three months before admission, with a mild attack of inflammatory rheumatsim. The patient was told at that time she had organic heart disease. Anæmia, dyspnœa, and cardiac palpitation were the chief complaints. Two days before admission she suddenly lost the power in her right arm and leg, with complete aphasia.

Physical examination showed mental apathy; an irregular heart with a loud mitral systolic murmur heard in the axilla and over the back. The spleen percussed large, but could not be felt. There was great hypersensitiveness of the trunk and of the extremities, especially on the right side, with paralysis of that side.

The course of the temperature curve was irregular, and ranged between 101° and 105°. The leukocytes showed an increase to 14,000 per c.mm., later falling to 10,000; there were 1,806,000 red blood cells, and 43 per cent. hæmoglobin. A culture from the blood showed micrococcus lanceolatus. Examination of the urine gave 6 per cent. of albumin (by volume), no casts. She passed from fourteen to twenty ounces during the twenty-four hours.

Upon *autopsy* the heart was found to weigh fourteen ounces; upon the mitral valve, extending to the anterior surface of the

auricle, and also into the ventricle, was a large patch of vegetation, rough and ragged, but not ulcerated; the heart muscle was mottled with pale areas. The spleen was swollen and soft, with numerous white infarctions The kidneys showed septic infarction. Of cultures taken from the spleen, liver, and kidneys, those from the first two organs showed abundant growths.

CASE VI.—Aged twenty-two years, female; book-keeper; admitted July 10, 1897; discharged August 18, 1897.

There was no family history. The patient had scarlet fever and mild rheumatism as a child. For the past two months she was anæmic and did not menstruate, although not pregnant. One month before admission mild rheumatic pains again appeared, soon followed by a sudden retinal hemorrhage. At the age of fifteen years she was told of the presence of a heart murmur.

Examination showed a pronounced thrill at the apex of the heart, with presystolic and systolic murmurs over the same area. The spleen was enlarged, urine normal.

The course of the temperature continued low and irregular, not going above 102°. The blood showed 10,000 leukocytes per c.mm. Culture gave a profuse growth of micrococcus lanceolatus; petechial hemorrhages developed with sharp pain, severe and sudden, over the region of the spleen, blindness in both eyes, and left hemiplegia, in which condition she died.

CASE VII.—Aged twenty-seven years, German, male; admitted April 1, 1903; died April 3, 1903.

For two months past the patient has been feeling weak and languid; four weeks before admission he was struck violently on the head; following this injury he felt chilly and feverish, had headache, earache, and at the time of admission he was delirious. Upon *examination* his neck was stiff and rigid, and painful upon motion; his extremities were rigid and painful also. Over the mitral area a systolic thrill and murmur were appreciable. The temperature continued high, 104°. There was no splenic tumor; there were no chills. Blood examination revealed micrococcus lanceolatus; the leukocytes were 9000 per c.mm. There was no Widal reaction.

At *autopsy* the mitral valve showed two large vegetations, a cyst on one segment and perforation of another. Under the pia and arachnoid, especially around the cerebellum, was a layer of greenish pus.

GROUP III. *A Case of Mixed Infection.*

CASE VIII.—Aged forty-four years, housewife; admitted January 18, 1902; died January 28, 1902.

The patient was a moderate alcoholic. The present illness began eight days before admission, with severe and protracted headache; three days before admission a hard, shaking chill occurred, followed by fever and sweating and increased prostration.

Physical examination showed marked conjunctivitis and rhinitis, prostration, and rigidity of the neck. The cardiac impulse was in the seventh space, and a mitral systolic murmur was evident. The spleen was enlarged. Lobar pneumonia soon developed. There were 21,000 leukocytes per c.mm. Culture from the blood showed growths of micrococcus lanceolatus and staphylococcus pyogenes aureus. Culture from the nose showed micrococcus lanceolatus, and one from the eyes showed staphylococcus. The temperature was fairly continuous from 103° to 104°, with frequent rises accompanied by chills. Upon lumbar puncture 23 c.cm. of cloudy fluid was obtained, from which smears were made, showing cocci arranged in pairs. The urine contained 4 per cent. of albumin, numerous hyaline and granular casts, and pus.

Upon *autopsy* a mass of polypoid vegetations was found on the mitral valve. The lungs contained a number of minute purulent nodules. The spleen showed numerous infarctions. A layer of pus covered the base of the brain; the ventricles contained turbid serum; the right lateral sinus and the right cavernous sinus were filled with clot. The ethmoidal and sphenoidal sinuses were eroded and filled with pus. The entire cord was bathed in creamy pus.

Group IV.

The following cases are of streptococcus origin:

Case IX.—Aged twelve years, female; admitted November 28, 1902; died December 2, 1902.

The patient had no previous illness of note. For the past four weeks she suffered from headache, pains in the back, languor, nose-bleed, irregular fever, indefinite chills, with sweating and vomiting; of late she had diarrhœa.

On *examination* the cardiac impulse was found in the anterior axillary line, and a loud systolic murmur heard over the entire left anterior chest, axilla, and back. The spleen was enlarged, urine normal, no eruption. The course of the temperature was irregular, from 101° to 105°, but there were no chills. There were 14,000 leukocytes per c.mm., and streptococcus pyogenes was found upon blood culture. No malarial organisms were found. The child became semicomatose and developed a right hemiplegia. No autopsy could be obtained.

Case X.—Aged twenty-four years, housewife; admitted August 12, 1897; died August 18, 1897.

There was a moderate alcoholic history. Eight days before admission and during her menstrual period the patient ate some indigestible food. She had pain in the abdomen, with vomiting, diarrhœa, and headache. She has vomited every day, and at one time the vomitus contained a little blood. She has had chilly sensations every day.

On *admission* there was a harsh mitral systolic murmur. Spleen not palpable. A few hemorrhagic spots were present. The temperature was enteric in character and continued at 105°. Leukocytes, 17,000 per c.mm.; no reaction to Widal test. Blood culture gave a growth of streptococcus pyogenes.

Autopsy revealed minute vegetations on aortic valve, and considerable mass of fibrin on the mitral, one cup being eroded and perforated. The heart muscle showed infarcts, as did the spleen and left kidney. The brain contained a blood clot as large as an egg in the right occipital lobe.

Group V.

The following are cases in which blood cultures failed to give results, and diagnosis rests upon pathological findings or clinical signs. Some of the cases occurred when the means of culture were not as perfect as at present, and some even before cultures came into general use.

Case XI.—Aged thirty-six years, female. Old malarial and rheumatic history; rheumatic arthritis, with chills and fever for seven weeks before admission. Splenic tumor, high remittent temperature, with chills; 10,000 leukocytes. Mitral, systolic, and presystolic and aortic diastolic murmurs present.

Upon *autopsy* one cusp of the aortic valve was hypertrophied and polypoid; there was cerebral embolism.

Case XII.—Aged forty-two years, female; history of œdema of extremities, and dyspnœa for years. Present attack of ten days' duration; temperature high and continuous; leukocytes, 27,000; no spleen, no chills, no cutaneous hemorrhages. There were mitral, systolic, and presystolic murmurs.

Autopsy showed thickening of the mitral and aortic valves, atheroma of the coronary arteries, and infarcts of the lung.

Case XIII.—Aged forty-four years, male; scarlet fever, diphtheria, malaria, and nephritis formerly; alcoholic and gonorrhœal history. Present attack of ten days' duration, with strain of the back and hæmaturia. Temperature was high, but irregular, with chills; there were petechial hemorrhages, but no spleen; leukocytes, 12,000 ; the urine contained a trace of albumin and a few casts. Physical examination showed a double murmur at the apex.

Autopsy revealed large vegetation on the aortic valve, and infarcts of both kidneys.

Case XIV.—Aged twenty-five years, male. Former malarial and gonorrhœal history. For six weeks before admission there was irregular fever, with chills and sweating; splenic tumor; 19,000 leukocytes; no petechiæ. There was a general systolic murmur. No autopsy.

CASE XV.—Aged twenty-nine years, female; scarlet fever as a child, with attacks of cardiac palpitation, dyspnœa, and œdema following. Temperature high and continuous; splenic tumor; cutaneous hemorrhages; leukocytes, 23,000; trace of albumin, and a few hyaline and granular casts. Systolic and presystolic mitral murmurs.

Autopsy showed mitral valve greatly stenosed; aortic valve greatly stenosed, with one cusp perforated; infarcts of the lung.

CASE XVI.—Aged forty-one years, male; old malarial history, with gonorrhœa and cystitis. Irregular fever, with chills and œdema of extremities; no spleen; no hemorrhages; urine contained 10 per cent. of albumin, hyaline, and granular casts. There was a mitral systolic murmur.

Autopsy revealed enormous vegetations on the mitral valve; infarcts of the heart, liver, and spleen.

CASE XVII.—Aged twenty-six years, male; old rheumatic history, alcoholic, with gonorrhœa. Ill three months with previous endocarditis. Temperature irregular, with splenic enlargement and cutaneous hemorrhages. Mitral, systolic, and double aortic murmurs.

On *autopsy* the mitral valve was thickened and retracted; the aortic eroded and calcareous; pericardium adherent. Infarcts of the spleen.

CASE XVIII.—Aged twenty-six years, male; rheumatic, alcoholic, gonorrhœal, and specific history. For eight days headache, diarrhœa, high, continuous temperature, splenic enlargement, and cutaneous hemorrhages. The urine contained 10 per cent. of albumin, hyaline, and granular casts. There was a mitral systolic murmur.

Autopsy revealed vegetations on both mitral and aortic valves, and infarcts of the kidney.

CASE XIX.—Aged forty-three years, female. Sudden onset, with chill, fever, diarrhœa, hemiplegia; temperature was continuously high; chill was not repeated; no splenic enlargement; no hemorrhages. Mitral systolic murmur.

Autopsy. Mitral valve thickened and retracted; infarcts of spleen and kidney.

CASE XX.—Patient was in coma when admitted; temperature 104.5°; no physical signs could be made out.

Autopsy revealed a large ulceration of the mitral valve.

CASE XXI.—Female. Former attacks of grippe and malaria. Upon admission there was swelling of the joints, fever, and coma. There were petechial hemorrhages, but no spleen; the urine showed 15 per cent. albumin, hyaline, and granular casts. No physical signs.

Autopsy showed thickening of the mitral valve and infarcts of the spleen and kidneys.

Case XXII.—Aged twenty-eight years, male. For two weeks had rheumatic pains, dyspnœa, and slight temperature; splenic enlargement; double aortic murmurs.

Autopsy showed ulceration and vegetations on the aortic valve; infarct of the spleen.

Case XXIII.—Aged twenty-eight years, female. Rheumatism with dyspnœa and cardiac palpitation for two months; temperature irregular; splenic tumor and hemorrhages; mitral systolic and aortic systolic murmurs.

Upon autopsy, vegetations upon the mitral valve and infarcts of the spleen and kidneys were found.

Case XXIV.—Aged twenty-four years, female. History of scarlet fever and diphtheria. Sudden onset of muscular pain, with irregular temperature, chills, and petechial eruption; albumin, 2 per cent. Mitral systolic murmur with a diastolic at base of the heart.

Autopsy showed vegetations on pulmonary valve, with perforation. Infarcts of spleen and kidney.

Case XXV.—Aged thirty years, female. Rheumatism starting with a chill, followed by fever and sweating; temperature continued high and irregular; splenic enlargement; 15,000 leukocytes; slight evidence of nephritis, and a mitral systolic murmur.

Case XXVI.—Aged forty-three years, female. For three months dyspnœa and œdema from a former rheumatic attack. Temperature high and irregular; leukocytes, 11,400; cutaneous hemorrhages and mitral systolic murmur.

Case XXVII.—Aged forty-eight years, male. Rheumatic attack of seven weeks' standing; temperature irregular, with chills, spleen, cutaneous bleeding, and 16,500 leukocytes. Albumin, 20 per cent.; large hyaline and granular casts. Mitral, systolic, and aortic diastolic murmurs.

Case XXVIII.—Aged thirty-three years, female. Sudden joint pains with vomiting and headache. Temperature irregular; splenic enlargement; leukocytes, 17,000; mitral systolic murmur.

Case XXIX.—Aged thirty-four years, male. Sudden onset with general pains, vomiting, chill, and sweating. Continuous fever, spleen, and petechiæ; 6000 leukocytes; mitral systolic murmur.

Case XXX.—Aged thirty-four years, male. Two months' duration, with headache and delirium. Continuous temperature, petechial hemorrhages, and mitral systolic murmur.

Case XXXI.—Culture gave staphylococcus pyogenes albus.

Autopsy showed vegetations of aortic valve and atheroma of the coronary arteries, infarcts of the spleen, petechial hemorrhages in all the viscera.

Case XXXII.—Aged thirty-one years, female. Sudden illness, with diarrhœa and headache; spleen, petechial hemorrhages, low and irregular temperature; 22,000 leukocytes; staphylococcus pyogenes albus were found upon culture.

Recapitulation.

From the accompanying cases it is evident that symptomatically there are a number of types of the disease.

One of sudden onset, short duration, with high continuous temperature, headache, splenic enlargement, cutaneous hemorrhages or bleeding from the mucous membranes, together with evidence of inflammation of the endocardium; here the endocarditis is but one manifestation of a severe general infection which rapidly goes on to a fatal termination.

The second form is of much longer duration, persisting for weeks, or sometimes for months, beginning gradually with irregular fever, which often becomes remittent or even intermittent, and may be accompanied by chills and sweating, gradual loss of flesh and strength; splenic tumor, hemorrhagic eruptions, abscesses, and endocarditis. This form is distinctly septic or pyæmic in its action, and presents an entirely different picture from the former.

A third class is one in which the chief factor is meningitis. Here we see signs of intense cerebral irritation, with the addition of endocarditis, enlargement of the spleen, petechial hemorrhages, septic infarctions, and often pneumonia.

Still a fourth variety is one in which the local endocardial signs and symptoms are of chief prominence, the constitutional affection being slight, except for the evidence of poor circulation.

The foregoing varieties are recognized by most authorities under the names of typhoid, septic or pyæmic, cerebral, and cardiac types, respectively, according to the predominance of the various symptoms.

There can, however, be no certain deductions drawn as to the variety of organisms causing the different clinical forms, for the conditions simulate one another too closely.

As examples of the typhoid form there are two of staphylococcus, one of streptococcus, and one of micrococcus lanceolatus infection (Cases II., III., X. and VII.).

As examples of the septic class of long duration there are 1 of streptococcus, 2 of pneumococcus, and 2 of staphylococcus infection (Cases IX., V., VI., I., and IV., respectively).

Of 3 cases of meningitis, 1 was of staphylococcus origin, 1 of mixed staphylococcus and pneumococcus origin, and 1 was of pure pneumococcus infection.

In 2 cases of pneumococcus infection there was neither pneumonia nor meningitis present.

The *endocarditis* is a pre-existing factor in most of the cases. There are instances, however, where there is no reason to suspect that a previous inflammation of the endocardium existed. We find cases where cardiac murmurs develop during the course of the disease, in which no abnormal condition existed in the heart at the

first examination. There are also numerous cases of ulcerative endocarditis, which run their course without giving any signs which would call one's attention to the heart. These are difficult of diagnosis.

In 19 of the 32 cases, the cardiac signs found upon physical examination were verified by post-mortem findings. They were mitral, 7 cases; aortic, 3 cases; mitral and aortic together, 6 cases; pulmonary, 1 case; mitral, aortic, tricuspid, and pulmonary together, 1 case ; these cases also showed affection of the heart wall in 1, adherent pericardium in 1, and sclerosis of the coronary arteries in 2.

While the greater number of murmurs represent lesions of the mitral and aortic valves, we must bear in mind that in malignant endocarditis more than in the simple form of the disease, we find evidence of endocarditis of the right heart, affecting the tricuspid and pulmonary valves.

Culture. In 24 cases from which blood was taken for culture, growths were obtained in 12. Cultures taken from the viscera of these cases which came to autopsy showed the same findings, and in no instance did the two results differ. One case showed pyogenic organisms taken from the viscera in which no blood specimen was taken. There were staphylococcus pyogenes aureus, 4; streptococcus pyogenes, 2; micrococcus lanceolatus, 3 cases; pneumococcus and streptococcus together, 1 case.

The cultures were all grown in bouillon or blood serum media. Bouillon is used exclusively now, and the best results are obtained from high dilutions.

The method of blood taking is as follows: Under strict antiseptic precautions a needle is introduced into the median basilic vein and about 10 c.c. of blood withdrawn. The needle is of fairly large calibre, and is attached to a glass tube holding 10 c.c., into which the blood runs of its own accord. The whole instrument when not in use is kept clean in a larger sterilized tube.

The culture tube is a large test tube holding about 50 c.c. of bouillon. To prevent contamination a piece of sterile gauze is placed over it, and on this a wire gauze which dips for about one inch into the test tube and is bent over the edges; over this again the cotton plug is inserted. Thus the plug can be removed without exposing the surface of the culture medium.

After the needle tube has been filled with blood 3 or 4 c.c. are expressed into the culture tube or flask—preferably the former—holding 50 c.c. of bouillon. Three such culture tubes are made.

The *temperature* may rise suddenly and remain continuously high, without remissions, until death ensues. This course of temperature is generally indicative of a severe infection of short course, and is unaccompanied by chills. It simulates closely the curve of typhoid fever, and is often the cause of mistaken diagnosis.

The temperature is frequently irregular, may be low or high, accompanied by remissions or frequently by intermissions, sometimes occurring daily, so that there is a daily rise and fall of five or six degrees. These marked remissions are often accompanied by chills and profuse sweats.

The irregular type of temperature accompanies the cases of considerable standing, although occasionally they are of but short duration.

The *blood* examination shows an increase in leukocytes in all of the cases; those of high continuous temperature being (with but one exception) over 15,000 per c.mm., and frequently 20,000, 25,000, or 30,000 per c.mm. A count of less than 15,000 per c.mm. belongs to the irregular and protracted group, although occasionally a member of this class exceeds that figure.

In Jackson's series of 59 cases he found the leukocytes regularly increased from 16,000 to 20,000 per c.mm. This increase does not hold in my series of cases, for I distinctly find in the septic varieties that the leukocytes are almost invariably below 15,000 per c.mm., and frequently below 12,000 or even 10,000 per c.mm. According to Babcock (*Diseases of the Heart*) leukocytosis is the rule; but where septicæmia exists, and there is but slight increase in the leukocytes or none at all, malignant endocarditis is to be suspected. The red blood cells and hæmoglobin show the changes of secondary anæmia.

Emboli are of frequent occurrence, but vary greatly as to the seriousness of their results. When occurring in the cerebral arteries, coronary arteries, or lungs they may be quickly fatal. They occur, however, most frequently in the spleen and kidneys. The lodging of an embolus is accompanied by sudden, sharp pain in the part affected, together with a rise of temperature and frequently a chill. Such an infarct is not infrequently followed by death of tissue and abscess, thus forming a new focus of infection. Among our nineteen autopsies there were sixteen showing emboli—one in the brain, two in the lung, one of the heart muscle, the others occurring in the spleen and the kidneys, together with one in the liver.

Hemorrhages occurred in 16 of the 32 cases enumerated here, the bleeding being mostly in small pinhead spots of the petechial variety, occurring in successive crops; in a few instances, however, larger ecchymoses were to be seen. Bleeding from the mucous membranes occurs, usually as epistaxis; less frequently we find hemorrhage from the lungs, from the kidneys, or into the brain.

In our collection there were 3 cases of hemiplegia; of these 1 was of staphylococcus origin, and 2 of pneumococcus origin.

Splenic enlargement occurred in about half of the cases cited here, with greater frequency, however, in the prolonged ones; palpation of the spleen often elicits pain from congestion or as the result of previous infarction.

Nervous Symptoms. In many cases apathy precedes delirium, which is of an active character, or is low and muttering; the active delirium occurs in cases of severe general infection of the typhoid type, while mutterings and hallucinations take place in the prolonged disease of septic type. Convulsions, coma, or death may occur at any time from embolism or hemorrhage of one of the cerebral arteries. With meningitis added, the nervous symptoms take on a more severe aspect, with cerebral irritability, convulsions, stupor, or coma; retraction of the head and neck; dilated pupils, which do not react; photophobia and strabismus; excessive hyperæsthesia; marked rigidity of the muscles of the back and extremities; opisthotonos, etc.

The pulmonary symptoms are those accompanying any severe endocarditis, and are caused by venous congestion of the lungs and insufficient oxygenation of the blood; they are evidenced by cyanosis, dyspnœa, cough, mucopurulent expectoration; moist rales may be heard in the dependent portion of the chest. With pulmonary infarct we have sharp pain, sudden dyspnœa, and hæmoptysis. In case death does not ensue, evidence of consolidation follows with, perhaps, pleuritic effusion or empyema. Where pneumonia occurs its characteristic signs are added to the above.

The *urine* generally contains a trace of albumin, with a few hyaline and granular casts; a few cases show a marked nephritis, possibly independent in origin, possibly due to the irritation of the tubules by circulating bacteria or toxins, or from infarctions; in 2 cases there was a considerable quantity of blood in the urine. Where emboli occur, with softening and abscess, pyuria results.

Concerning the use of antistreptococcus serum I have collected from the literature 24 cases; 7 have resulted in recovery, and 17 have died. In some the recovery seemed to follow the injection of the serum; in others the injection apparently did no good, or did decided harm. Beneficial results have been obtained in enough cases to warrant its receiving a more thorough trial.

Summary.

1. Malignant endocarditis is a disease of bacterial origin; it differs from single acute endocarditis in the extent of endocardial inflammation and tissue necrosis; in the fact that the right heart is more often attacked; in the more frequent embolic processes which are septic in character. Micro-organisms are found in the blood during life, in the emboli, and on the heart valves after death.

2. There is nothing in the clinical appearance distinctive of any particular variety of germ causing it.

3. Primary cases are rare, though they do exist; most cases, however, accompany rheumatism, septicæmia, the acute infectious diseases, or are engrafted upon an old endocarditis.

4. Almost all are fatal; the ones due to severe infection in a few days; the septic ones in a few weeks. The first variety have a leukocytosis of 15,000 or over, the latter usually below that number, some being very slight.

5. Emboli and hemorrhages are of frequent occurrence, and may be fatal in their results.

6. The urine usually shows evidence of nephritis; it may contain blood and pus from hemorrhage or infarct.

7. Treatment is usually unavailing, excepting the serum therapy, which is of uncertain value.

8. Infants and young children seem to be almost exempt from the disease.

The thirty-two cases cited here were published at greater length in the *Report of the Presbyterian Hospital* (New York) for 1904; they occurred in the hospital during the past ten years.

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ANGIONEUROTIC ŒDEMA.

REPORT OF TWO CASES WITH THE HISTOLOGY OF A PORTION OF THE GASTRIC MUCOSA OBTAINED BY THE STOMACH-TUBE.

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(From the Clinic of Internal Medicine, Dr. Dock.)

In recent years considerable attention has been given to a disease which was first described accurately in 1882 by Quincke,[1] who gave to it the name "acute circumscribed œdema of the skin." Strübing,[2] an early student of this disease, proposed "angioneurotic

œdema" as a more fitting designation for the symptom-complex, basing his choice on the supposed etiology of the condition. The latter name is the one by which it is generally known at present. It is a disease characterized by transient swellings in various parts of the body, as, for example, in the skin of the extremities, of the face, in the mucous membranes of the mouth, pharynx, and larynx. Severe gastrointestinal symptoms of comparatively short duration often accompany the visible swellings or alternate with them. Heredity plays a prominent role in the etiology; the duration of the disease is variable, but usually chronic. It is not my purpose, however, to discuss the various manifestations and phases of angioneurotic œdema—a disease which, in many of its aspects, still belongs to the future for determination, but rather to call attention to the gastric features of this condition, drawing particular notice to Case II., in which it has been possible for the first time, in so far as I can determine, to make a histological examination of the gastric mucosa during an attack involving the stomach. To this end the following histories are given:

Case I.—F. B., a farmer, American, aged thirty-nine years, married, was brought to the University Hospital by Dr. Snyder, of Hanover, Michigan, on June 21, 1904. The following notes were dictated by Dr. Dock while examining the patient with the clinical staff:

The patient complains of pain in the epigastrium and swelling in different parts of the body. He describes the pain as beginning in the epigastrium and spreading sometimes around to the right side, but never into the shoulder-blade or shoulder or downward. He has had these pains as long as he can remember; they come on without cause, and are accompanied by nausea and vomiting. He has them about once a month, at times as often as once a week; they have been somewhat more frequent this year than formerly. The pains last four to five hours. Morphine alone relieves them. By the next morning he is always ready to go to work.

As long as the patient can remember he has also had attacks of swelling in the hands and feet, rarely in the face, but he has had the eyes swollen shut, *e. g.*, one week ago, when the upper lip was also swollen so that it was about one inch thick. He has also had swelling of the larynx so that he can hardly speak; sometimes he feels swelling without pain in the epigastrium; sometimes feeling of "clogging" under the sternum. At times the penis swells. The tongue is never swollen. About twenty years ago he had hæmaturia; he does not remember what the blood looked like, but thinks it was present in the urine about one week. He thinks he has passed no blood since then, but the urine is "usually red." Two or three times this year he has passed blood in the stools. The general health of the patient has not been affected. Weight and strength show no change.

Status Præsens. Patient has a large frame, moderate panniculus; muscles large, but rather soft. Skin over body of natural color. Face, neck, and ears very red. Nose, cheeks, and chin show many enlarged venules. Slight rosacea of nose. Over right hand and wrist skin shows large pigmented areas, with red between, but no swelling. The left hand and forearm are swollen and the skin is red; there is a slightly elevated red patch on the front of the forearm, from the upper one-third and from the inner side to the line of the radial artery. The ball of the thumb is considerably swollen, feeling thicker and tenser than the right thumb and showing the marking of the epidermis more plainly. Palmar surface of left thumb is tense, red, and cyanotic. On back of hand moderate swelling, but not very much redder than right hand. Patient says there is itching when the swelling begins; otherwise feels nothing abnormal but a sense of tightness. Color of hands not much affected by a change of position.

Thorax is well formed; upper part of sternum and costal cartilages rather prominent; lower part of sternum slightly depressed. Epigastric angle very wide. Apex beat not distinctly seen, but there is a pulsation in the fourth intercostal space one inch inside the nipple. Heart dulness begins on the fifth rib, extends from left parasternal to left sternal line. Auscultation: heart sounds moderately strong and clear. Radial pulse: artery easily felt, is not tortuous, no irregular thickening; pulse rather small, regular, tension low.

Abdomen is on a level with the ribs in the middle, sloping slightly on the sides. The abdominal wall is rather firm, but without local rigidity. Patient does not complain of deep pressure in epigastrium or gall-bladder region, where palpation and percussion are negative. No tenderness in the back.

The patient has had trouble with his teeth for a long time. Many of them are missing; those present are mostly carious. Gums are rather spongy, with some ulceration, especially in the lower jaw.

The diagnosis of angioneurotic œdema was made, and the patient was advised to remain under the care of his home physician, and to take four minims a day of a 1 per cent. solution of nitroglycerin.

Case II.—G. W. S., a stenographer, American, aged twenty-one years, single, entered the medical clinic of the University Hospital on October 23, 1903, complaining of swellings of the hands, legs, and larynx, and of "stomach trouble."

Family History. The patient's father is living and in good health. His mother is living, but has swelling of her hands similar to that of the patient; she also has stomach trouble. The patient has two brothers living and well. His mother gave birth to one stillborn son. One sister is living; any blow on her face will cause it to swell. Another sister died at the age of eighteen months of "epilepsy." Maternal grandmother living and in good health at the age of

eighty-three years. Maternal grandfather died of unknown cause. Nothing was known of the paternal grandparents. No history of importance in other relatives was obtained.

Personal History. The patient had "mumps" at the age of twelve years. Later he had "measles" and "chicken-pox." Good recovery in each instance. When seventeen years old he had "scarlet fever," complicated with "nephritis;" since then he has been well, with the exception of the present disease.

History of the Present Disease. The patient first noticed a swelling in the hands when he was twelve years old. He thought it was due to "overheating his blood." The swelling did not last long, and the patient could not tell when it was coming on; it usually disappeared within forty-eight hours. Sometimes it came on after exertion; at other times the same amount of work caused no swelling. Later swellings appeared in his feet, then in his knees and elbows. Patient says the swelling seems to be more in the joint than in the muscles. Riding a bicycle has caused swelling of the scrotum and then of the penis. The symptoms gradually became worse. Since the attack of scarlet fever the patient's throat has troubled him, his voice being husky at times. Four years ago the patient had "œdema of the glottis," and tracheotomy was performed. He was unconscious at this time. He was confined to his bed for three weeks after the operation, during which time he says his temperature once reached 106°. While in bed the skin on the palms peeled off. It was at this time that his doctor told him he had had scarlet fever; the urine became black, and the specific gravity was 1.008, according to the patient. It was about two months before the tracheotomy wound healed; previous to the healing there was a discharge from the wound with a "fierce" odor. His throat at this time was so sore that he could eat no solid food. After recovering from this illness the patient was in fairly good condition, except for occasional swellings, until April, 1903, when he had another attack of œdema of the glottis. This came on in the morning. At noon he was unable to eat his dinner, and at 6 P.M. of the same day he was unconscious, and a second tracheotomy was performed. On July 13, 1903, the patient noticed a swelling "under the shoulder-blade" on rising in the morning. He says this gradually worked up his back, and he noticed swelling in his throat about 4 P.M. of the 13th. At this time he used a gargle containing carbolic acid. After eating supper he gradually became worse until midnight, when intubation was tried. This failed, and a trocar was thrust into the trachea. He was in bed five days at this time. About the middle of August, 1903, he again had symptoms of œdema of the glottis, which subsided with steaming. At times coincident with the swelling in the skin the patient suffers from nausea, vomiting, and sharp pain in the epigastrium, lasting one to two days. He can assign no definite cause for these attacks.

The patient is obliged to do light work, avoiding much exercise, because of the liability to produce swelling. He takes his meals regularly. Appetite is good. Does not use tobacco. Uses alcohol very moderately. He drinks tea and coffee with his meals.

On admission to the hospital at 8.30 P.M. on October 23d, Dr. Alexander noted a puffiness all over the right hand and foot, especially well marked on the palmar surface of the thumb. No œdema in left hand or foot. A few slightly raised red patches over thorax, more numerous over sternum. Irregular, red, slightly raised patches over abdomen. Skin over the rest of the body of good color, elastic, slightly moist. Temperature, 97°; respirations, 24; pulse, 72.

October 24, 1903. Laryngoscopic examination by Dr. Dock. Larynx is small; epiglottis straight, but curled from side to side. Interarytenoid space deep. Entire mucous membrane red and slightly swollen. False vocal cords project inward, almost covering the true cords in phonation. Cords slightly red. Trachea small, moderately congested. Blood pressure (Riva Rocci) 138 mm. Hg. Nitroglycerin gtt. j of a 1 per cent. solution, ordered every three hours. After two doses (7 P.M.), pressure (Riva Rocci) 134 to 137 mm. Hg. Blood examination shows 4,560,000 red cells, 10,186 whites, and 100 per cent. of hæmoglobin.

25*th*. *Status Præsens:* Temperature, 98°; respirations, 20; pulse, 76, regular, moderate rise, good tension. Systolic pressure with Cook's modification of the Riva Rocci apparatus, 125 mm. Hg. at 10 A.M. Patient is in active dorsal position; mind is clear, expression natural. Usual weight, 145 pounds. Before second tracheotomy (April, 1903) weighed 160 pounds. Present weight, 146 pounds, stripped. Height, 5 feet 11¾ inches. Patient is well built, frame fairly strong. Panniculus small. Muscles fairly developed and firm. Below the right angle of the jaw is a body about one and one-half inches long, of the thickness of a lead-pencil, which runs from below upward and backward; surface slightly uneven, no pulsation in it. Lymph glands negative. Slight swelling on dorsum of left hand over the carpal and bases of the metacarpal bones. Skin not red or shiny here. Same condition on sole of left foot, especially over the base of the great toe. Right hand and foot negative to-day. Joints otherwise negative. Skin shows slight flush over thorax. Acne eruption of moderate extent over shoulders. The rest of the skin is of good color; moist.

Pupils equal, react well. Sclerotics clear. Conjunctivæ of good color. Lips show trace of cyanosis. Teeth are in good condition. Tongue is moist, not swollen; has very thin, white coat. Voice is husky; can scarcely speak above a whisper.

Neck shows a scar about 3 cm. long, the width varying from ¼ to 1¼ cm. It is situated in the middle line just below the thyroid cartilage; skin pinkish over it. On swallowing the lower half of the

scar moves upward, being attached to the structures beneath. Right lobe of thyroid gland palpable; left not palpable.

Thorax well formed. Expansion good and symmetrical. Percussion note slightly higher pitched and less resonant over upper left front; otherwise negative. Auscultation gives slightly increased vesicular over left apex anteriorly; with this exception normal vesicular throughout. Auscultation of spoken voice negative.

Heart: Apex just visible and palpable in fourth intercostal space in the nipple line. Dulness slightly increased to the left. Both sounds heard well at apex; the first is followed by a very faint, soft, blowing murmur, which is not transmitted into the left axilla, but is heard in the third intercostal space at the left edge of the sternum. The second sound at the apex is clear. Pulmonic area: sounds clear, no accentuation. The first aortic sound is replaced by a very faint blowing murmur, which is not heard under the sternum. First sound at tricuspid area roughened.

Abdomen is just below the level of the ribs and is symmetrical. Walls moderately tense. Spleen and liver not palpable. No tenderness.

Toward the end of the examination the skin of the thorax showed a mottled erythema.

Examination of stool: large, brown, consistency of thick soup, some foam; odor foul; small amount of mucus; a few leukocytes; no red blood cells.

Urine: Day sample (7 A.M. to 7 P.M.) amounted to 800 c.c.; specific gravity 1.013; reaction neutral; slightly turbid; sediment was small in amount and contained a few polynuclear neutrophiles. Night sample (7 P.M. to 7 A.M.), 120 c.c.; specific gravity 1.030; neutral, pale yellow, moderately turbid; sediment large in amount, and contained many leukocytes and a few cylindroids. In both samples tests for sugar were negative; a trace of albumin was found in the night sample; no casts; no erythrocytes.

26th. Urine presented similar macroscopic and microscopic appearances. A differential count of the white cells of the blood showed the following percentages:

Lymphocytes	22.09 per cent.
Mononuclears	8.48 "
Transitionals	2.95 "
Polynuclear neutrophiles	64.01 "
Polynuclear eosinophiles	2.36 "

At 7.30 P.M. several fresh drops of blood were examined for filaria, no parasites being found.

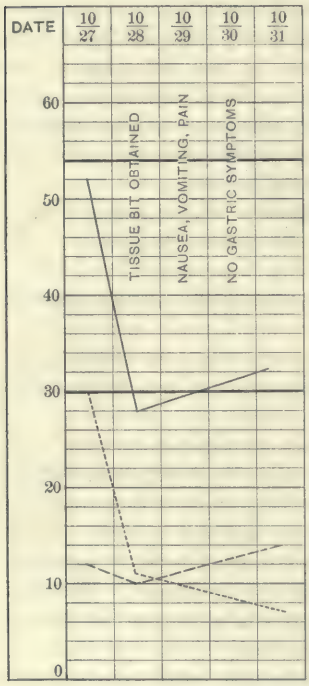
27th. Patient given an Ewald test breakfast. It remained in the stomach one hour, at the end of which time 100 c.c. were obtained. Had normal stomach odor. Contained an excess of mucus. Peptic digestion 8.5 (Mett) in ten hours. The fluid, examined chemically, showed free HCl, 30; loosely combined HCl, 12; total acidity, 52.

The microscope showed a moderately large number of leukocytes. The swelling of the left hand and foot has largely disappeared to-day.

The urine of October 27th and 28th continued to show leukocytes; otherwise it was negative.

28th. The patient complains of severe pain at the end of penis on micturition. This has been bothering him for the last few days, and is worse to-day. Ewald breakfast given. Remained in stomach one hour and five minutes; 130 c.c. were obtained. Lavage showed blood and a large piece of tissue. Odor normal. Free HCl, 11; loosely combined HCl, 10; total acidity, 28. No lactic acid; peptic digestion 2.2 mm. in nine and one-half hours. Microscopic examination revealed a few yeast cells.

FIG. 1.



The acidity of the gastric contents represented in cubic centimetres of $\frac{N}{10}$ NaOH.

Dotted line: free HCl.
Broken line: loosely combined HCl.
Continuous line: total acidity.

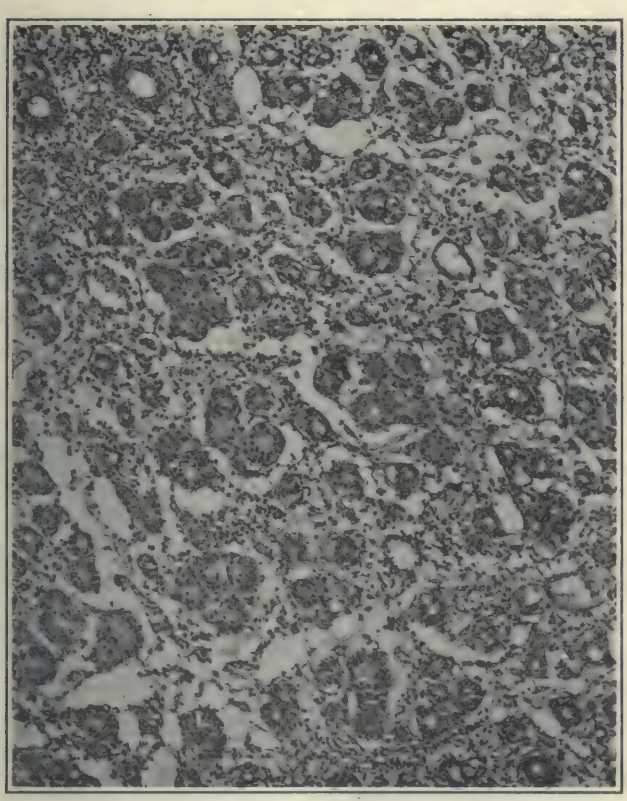
29th. Patient did not sleep well. At 7 A.M. felt sick at his stomach, and refused Ewald test breakfast. During the forenoon and early afternoon the patient vomited a light-greenish fluid several times, and complained of pain in his stomach. At 3 P.M. the stomach-tube was passed and the organ was washed. The patient did not vomit again until 8 P.M., having slept about an hour previous to this time. At 11 P.M. the patient was extremely nauseated and vomited considerably. Says he often has these attacks, lasting one to two days. Retching and vomiting continued, and at 1 A.M. on October 30th the stomach was washed again. Washings showed an excess of mucus; no solid particles.

The leukocytes in the urine now became about equally numerous in day and night samples. The microscopic examination showed a good many red blood cells in a mass resembling a small clot, only a few cells being scattered through the field, and a moderate number of leukocytes. In a preparation stained with methylene blue a few polynuclears and many small, round, epithelial cells with centrally placed nucleus, both singly and in patches. Many cellular casts; the latter were still present on the following day. Albumin about 1:30 by volume.

30*th*. Patient feels better to-day. Nausea, vomiting, and pain in epigastrium have ceased.

31*st*. The patient received a third Ewald breakfast to-day. This remained in the stomach one hour and five minutes; amount, 100 c.c. Chemical examination, quantitative, showed free HCl, 6; total acidity, 32.

FIG. 2.



Portion of gastric mucosa removed by stomach-tube from Case II. of angioneurotic œdema. Extreme œdema of stroma.

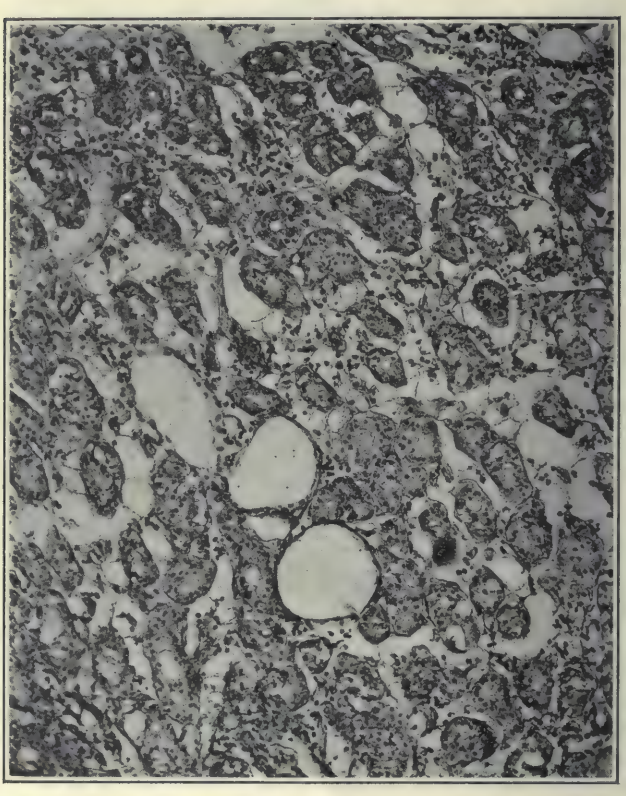
The condition of the patient remained unchanged up to November 2, 1903, when he left the hospital.

The piece of tissue which was obtained in the stomach washings from Case II. on October 28th was placed immediately in absolute alcohol and sent to the pathological laboratory for examination. The report which Dr. Warthin has made follows:

Tissue received from Dr. Dock's clinic with following description: "Semitranslucent, almost jelly-like bit of tissue obtained from

stomach washing of patient S. Put at once into strong alcohol." The tissue was examined by me in alcohol as soon as received. The bit measured 13 mm. in greatest length, 7 mm. in greatest breadth, and 4 mm. in greatest thickness. It was soft, white, smooth on one surface and slightly rough and ragged on the other, suggesting a portion of the mucous membrane. The size of the

FIG. 3.

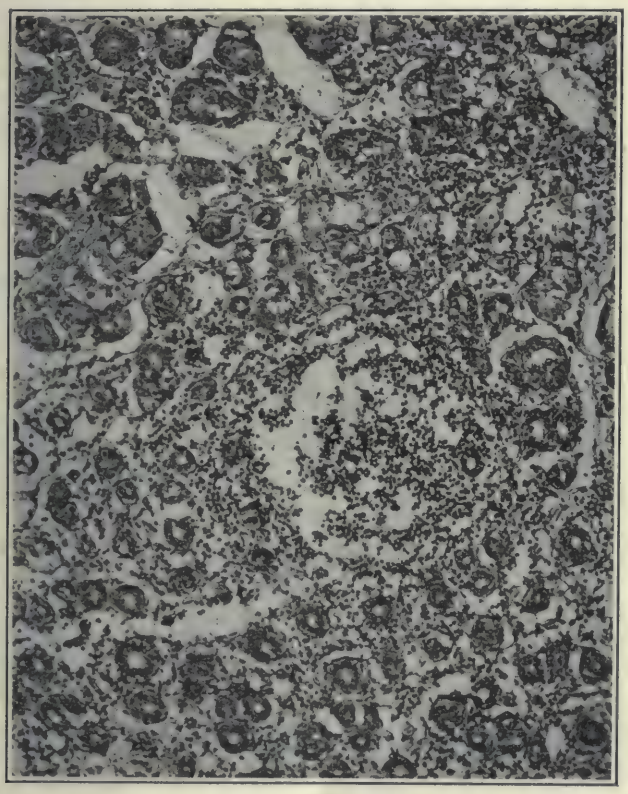


Portion of gastric mucosa removed by stomach-tube from Case II. of angioneurotic œdema. Extreme œdema. Great dilatation of lymph spaces and vessels.

bit was, however, taken as an argument against its being a portion of the gastric mucosa, as of the many bits obtained from stomach washings examined in the laboratory none had ever approached this in size. The tissue was embedded in paraffin and stained in hæmatoxylin and eosin, Van Gieson's, and kresyl-echt-violett. Microscopic examination showed, however, that the piece was gastric mucosa, most probably from the pyloric end, as few parietal cells were found in the glands and as numerous lymph nodes were

present, the character of the sections corresponding in general to that of glands from the pyloric end of the human stomach. The entire tissue presented the picture of an extreme œdema of the interstitial tissue, the lymph spaces and vessels being enormously dilated, the cells of the stroma being separated by wide spaces or vacuoles and the supporting fibres in many places separated into their ultimate fibrillæ. The glands as a rule were somewhat loosened

Fig. 4.

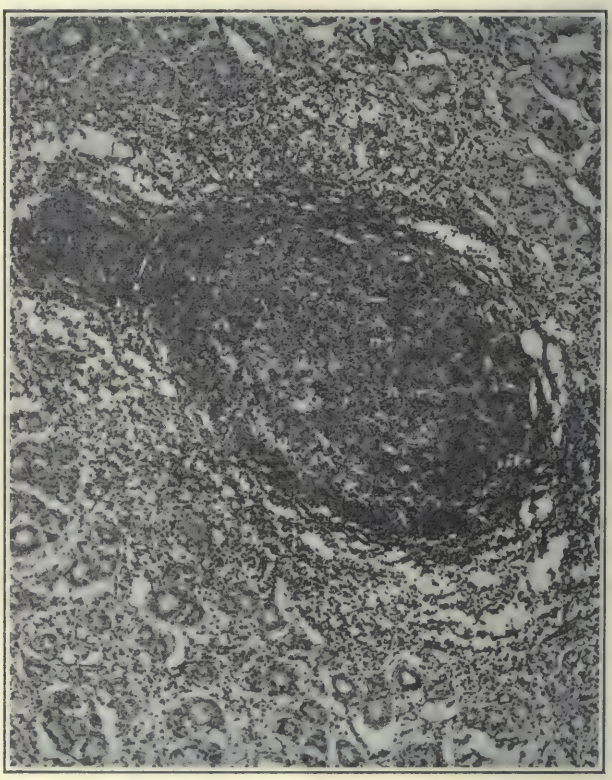


Portion of gastric mucosa removed by stomach-tube from Case II. of angioneurotic œdema. Small lymph follicle, showing marked œdema.

or contracted from their basement membranes and vacuoles were found in some of the epithelial cells. No excess of mucous formation. The œdema, however, was chiefly confined to the interstitial tissue, hence the suspicion of the tissue having been water-soaked, which was entertained at first sight, was not supported. The appearance of the vacuoles in the stroma and the dilation of the lymphatics gave, moreover, the impression of a fluid confined under pressure. A very finely granular precipitate staining red with eosin in the

lymphatics and about the edges of the vacuoles was taken as evidence of the slight albumin content of the fluid. Numerous small round cells were present in many areas, to a greater extent than is usually found in normal gastric mucosa. Many of the stroma cells contained vacuoles and were spherical and swollen. The smaller lymph nodes showed likewise an extreme œdema, the cells being widely separated. In the larger lymph follicles the œdema was

FIG. 5.



Portion of gastric mucosa removed by stomach-tube from Case II. of angioneurotic œdema. Large lymph node, showing œdema of the peripheral and central portions.

most marked about the periphery of the node and in the central portion, the cells in these places being widely separated. From all the appearances a diagnosis was given of "extreme œdema of gastric mucosa, non-inflammatory in origin."

As we see from this report, the possibility of the tissue being water-soaked was considered. This is excluded, however, not only by the practical limitation of the œdema to the interstitial tissue, but also by the fact already mentioned, namely, that the tissue was

placed in absolute alcohol as soon as it was removed from the stomach. Incarceration of the mucosa within the end of the stomach-tube is another possibility which it is necessary to keep in mind, but which can be dismissed in the present instance, as the removal of the test meal with the subsequent lavage was performed by an experienced operator. As the piece of tissue was undoubtedly obtained from a wound inflicted by the end of the tube at the time when the stomach was being washed, the conclusion is forced upon one that there was an acute, non-inflammatory œdema of the gastric mucosa.

Œdema has been looked upon from the first as the probable cause of the gastric symptoms so frequently associated with angioneurotic œdema. Quincke,[1] reasoning from analogy, looked upon the nausea, vomiting, and pain as manifestations of local œdema of the stomach. He says, "Auch auf Magen- und Darmschleimhaut dürften, nach den in einem Falle anfallsweise auftretenden gastrischen und intestinalen Symptomen zu schliessen, solche umschriebenen Schwellungen vorkommen." It is possible, also, that the periodic vomiting described by von Leyden[3] is to be attributed to œdematous swellings of the wall of the stomach. Attacks of colic of obscure origin have recently been shown by Osler,[45] to be manifestations of the erythema group of skin diseases, in which angioneurotic œdema is included. Strübing[2] considered the gastrointestinal symptoms the result, in part, of a local œdema, though unwilling to admit that œdema may explain all the symptoms on the part of the digestive tract; nor is it possible to disprove his view. Osler[6] was among the early writers upon the subject to indicate the probability of the stomach and intestinal symptoms being due to a local œdema; a view which he has recently reaffirmed. Fox[7] says: "It is generally conceded that the bronchial mucous membrane may be involved and a true asthma result, coinciding or alternating with outbursts of cutaneous urticaria. The implication of the digestive tube is less certain; but many authors, such as Guéneau de Mussy, accept the doctrine and thus explain certain intestinal attacks characterized by pains, diarrhœa (sanguinolent or not), melæna, or tympanites. Drs. J. J. Pringle and Hillier Chittenden have recorded cases of hæmatemesis suspected to own a similar cause, and Dr. Galloway has observed a wheal in a rabbit's stomach." Many other instances in the literature might be cited in which the nature of the gastrointestinal disturbances in angioneurotic œdema was similarly surmised.

The fall in free hydrochloric acid and in the total acidity coincident with the development of the stomach symptoms in Case II. may have been due to œdema of the mucosa. It is possible that the pain may also be explained by a stretching or pressing of the nerves or nerve endings.

As far as I have been able to determine from a careful review

of the literature, this is the first case of angioneurotic œdema in which it has been demonstrated that an œdema existed in the mucous membrane of the stomach synchronously with an attack of nausea, vomiting, and pain. Galloway's finding in the stomach of a rabbit is the only comparable instance which I have met with. My efforts to consult his original article have been unsuccessful. To conclude that all attacks of gastric disturbance met with in acute circumscribed œdema are attributable to local œdema of the stomach wall would be unwarrantable. To assume that a simple, non-inflammatory œdema is the only pathologico-anatomical alteration which may occur in the stomach in this disease would be equally unjustifiable. We can state positively, however, that simple œdema of the stomach wall does occur concomitantly with attacks of nausea, vomiting, and epigastric pain at times, at any rate, and that the probability of local œdema lying at the base of practically all of the gastrointestinal symptoms in angioneurotic œdema is greatly strengthened by this report.

It is with pleasure that I acknowledge my indebtedness to Dr. Warthin for the time and labor which he devoted to the preparation of the accompanying photomicrographs.

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PRIMARY CARCINOMA OF THE DUODENUM.

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Text-books, systems on internal medicine with few exceptions, and even monographs on diseases of the intestines, are singularly silent or give very little attention to malignant neoplasms of the duodenum. Indeed, such tumors occur in that part of the intestine

very rarely, but sufficiently often to give occasion for study. It is a suggestive, yet noteworthy fact, that malignant disease for the most part spares the small intestine, and, on the other hand, revels in its attacks on the stomach and the large intestine. The pylorus and the ileocæcal valve mark the limits between which tumors of a malignant nature are rarely seen, while, on the other hand, the structures forming these limits are more or less frequently involved; that is, the pylorus and the ileocæcal valve (the latter especially on its colonic surface) themselves are not infrequently the seats of a carcinoma. Cuneo and Lucène,[1] who have done much anatomical work on the lymphatics of the stomach, analyzed ten specimens of pyloric carcinoma, and in all but one found the pyloric valve the limit of invasion and growth; in only one of these specimens did the carcinoma extend from the pylorus into the duodenum. Similarly at the other end of the small intestine, while the colon is relatively not infrequently the seat of carcinoma, the ileocæcal valve forms almost a barrier to the extension of carcinoma into the ileum. When primary malignant disease does attack the duodenum or the ileum it starts from those portions of the gut much more frequently than it extends from the pylorus or the cæcum.

Frequency of Primary Malignant Disease of the Small Intestine. In Guy's Hospital between 1826 and 1893 there are records of 17,652 autopsies. Perry and Shaw[2] investigated these, and report ten cases of malignant disease of the duodenum; of these ten cases, four were carcinoma, six were sarcoma.

Fenwick[3] states that in searching the records of the London Hospital's autopsies, amounting to 19,518, the duodenum was found to be the seat of malignant growth in 18 cases.

Leichtenstern[4] gives some statistics concerning the relative frequency of carcinoma which will illustrate the relations between carcinoma of the various divisions of the intestinal tract. He says that between the years 1858 and 1870 there were 34,523 deaths at the Vienna General Hospital, of which 1874 were from cancer of different kinds. He examined the records of 4567 cases of cancer at the same hospital, and found 143 were of the rectum and 35 of the rest of the intestinal tract. Omitting cases of cancer of the rectum, he collected from published cases, records of pathological institutes and hospitals, 154 cases of intestinal carcinoma, 33 of which were of the small intestine, comprising 17 of the duodenum and jejunum and 16 of the ileum. He states that the small intestine furnishes 4.3 per cent. of the cases of cancer of the intestines in general. Utilizing his calculation and including his 616 cases of rectal cancer, we find that in 770 cases of intestinal carcinoma there were 33 of the small intestines.

From the years 1870 to 1881 inclusive, 20,480 autopsies were made at the Pathological Institute of the Vienna General Hospital, of which Maydl[5] reports 1460 were cases of cancer. Of these, 100

were cases of intestinal growths, in which the duodenum was involved only in 2 cases, the jejunum in no case, and ileum in 4 cases.

Nothnagel[6] adds to Maydl's statistics, and reports that at the same hospital between 1881 and 1893 inclusive, there were 21,358 autopsies, of which 2125 were on cases of carcinomatous growths. Of these, occurring somewhere in the entire intestinal tract, were 243, of which 5 occurred in the duodenum, none in the jejunum, and 6 in the ileum.

A. Zemann[7] from a collection of 21,624 autopsies, reports 165 intestinal carcinomata, 9 cases involving the small intestine, of which 3 involved the duodenum, none the jejunum, and 6 the ileum. These statistics come from the source from whence Nothnagel derived his.

Bryant[8] collected the reports of 110 autopsies of cases of carcinoma of the intestinal tract, of which 6 involved the small intestine. Of these I have been unable to find out how many were of the duodenum.

Müller,[9] examining the records of 5621 autopsies conducted at the Pathological Institute in Berne between the years 1886 and 1891, found 521 cases of carcinoma, of which 41 were intestinal; of these, 9 occurred in the small intestine, that is, 6 occurred in the duodenum, and 3 in the other parts of the small intestine, probably in the ileum, a relatively larger number than in the Vienna statistics.

Georg Heimann's[10] statistics, which are very exact and reliable, show that during the years 1895 and 1896 there died in the general hospitals of Prussia 20,054 patients with cancer, of whom 1706 had some part of the intestinal tract involved; of these, only 20 were of the small intestine, the number attacking the duodenum not being specifically mentioned. The last statistics are perhaps the most accurate and voluminous of any cancer statistics yet collected.

Lubarsch[11] examining the records of autopsies on deaths from carcinoma in the Pathological Institute of the Hospital of Breslau, reports 569 cases of carcinoma, among which 38 were in the large intestine, 2 in the duodenum, and 2 in the ileum.

Computing from the number of carcinomata of all organs collated by Maydl,[5] Nothnagel,[6] Müller,[9] G. Heimann,[10] and Lubarsch,[11] which amounted to 24,160 cases, we find that the general intestinal tract was involved 2128 times, 50 of these being due to carcinoma of the small intestine; in other words, carcinoma of the small intestine occurs in 2.3 per cent. of the cases of carcinoma of the intestinal canal, a figure much smaller than Leichtenstern's[4] statement of 4.3 per cent.

Or, even when using the statistics from all the previously mentioned sources, including Leichtenstern's[4] 794 intestinal cancers, but omitting A. Ziemann's,[7] whose cases were collected from the same source as Nothnagel's,[6] and adding Bryant's,[9] 110 intestinal carcinomata, we find that of 3563 cases of intestinal cancer 89 cases

involved the small intestine, or 2.5 per cent. of the whole. In either case the figure is lower than Leichtenstern's,[4] and still lower than Leube's[12] estimate, who says that carcinoma of the small intestine furnishes about 5 per cent. of all intestinal carcinoma.

We find among these cases an entire absence of specific statements of carcinoma of the jejunum.

Too much importance, further, should not be placed on deductions from statistics in determining the relative frequency of duodenal and ileal carcinoma, because there is some doubt as to the category under which carcinomata of the ileum have been placed. The most of the cases of carcinoma of the ileum occur in the region of or involve the ileocæcal valve, and on that account are classified by some as malignant disease of the small intestine, by others as of the large intestine.

In determining the frequency of carcinoma in the anatomical divisions of the small intestines we may use of the foregoing statistics only those of Maydl,[5] Nothnagel,[6] Müller,[9] and Lubarsch,[11] as the others do not specifically mention the occurrences of carcinoma in each division of the small intestine. Making this computation, we find of 4675 carcinomata, 15 occurred in the duodenum, or 0.3 per cent. of all intestinal cases, and 15 occurred in the ileum, or likewise 0.3 per cent. of the whole.

Rolleston[13] makes the statement that "the larger number of the recorded cases of malignant disease of the small intestine is found to start in the duodenum and, according to some statistics, three-quarters of the cases of malignant disease of the small intestine occur in the duodenum." This is hardly borne out by an analysis of the recorded cases and statistics. While it is true that sarcomata have their seat of preference in the small intestines, it is also true that primary sarcoma of the small intestine is much rarer than primary carcinoma of that portion of the digestive tract. Thus, Müller reports only 1 case of intestinal involvement in 102 cases of sarcoma and 41 primary intestinal carcinoma out of 521 cases of carcinoma. Nothnagel[6] in a like manner says that of 274 cases of sarcoma, 3 occurred in the intestine, and among 61 lymphosarcomata, 9 occurred in the intestine. Of the three sarcomata reported by Nothnagel, 1 occurred in the ileum, 1 in the cæcum, and 1 in the rectum; and of his 9 lymphosarcomata, 1 involved the duodenum, 3 the jejunum, 3 the ileum, and 2 the cæcum. Libman,[14] it is true, collected 15 cases of sarcoma of the duodenum, yet his cases cover most all the sarcoma of the intestines reported in which the location is stated—41 in all.

Our review of statistics does not conform with the statements of Rolleston and of many of the various authors of monographs on intestinal diseases who claim that carcinoma of the duodenum is decidedly more frequent than carcinoma of the ileum. Even such a pathologist of most extensive experience as Birch-Hirschfeld, in

the first edition of his renowned *Lehrbuch der Pathologische Anatomie,* made the same statement, but changed it in the third edition to represent the state of facts nearer the truth, by reversing his original statement and thus giving the ileum the site of greater preference for carcinomatous attack over the duodenum.

From the consideration of these statistics a fair statement would indicate that carcinoma of the duodenum occurs not more frequently than carcinoma of the ileum, that the one is as infrequent as the other, and that both are rare; that carcinoma of the jejunum is practically unknown.

The Division of the Duodenum Most Affected. In considering the topics connected with the specific observations as to the situation of the carcinoma in the duodenum, as to the variety of carcinoma, and so on, most of the later writers on duodenal carcinoma have made use of the valuable series of cases collected and reported by Whittier[15] and Pic.[16] Whittier,[15] in 1889, gathered 13 cases which had not previously been connected with any published article on the subject of duodenal carcinoma, and Pic, in 1895, 10, but of Pic's cases 2 were previously included in Whittier's series. In these two collections 21 cases are, therefore, distinct. The great trouble with deductions from statistics of cases gathered by various authors is the danger arising from utilizing the totals gathered by each and summing them up as so many individual cases; in this way a single case may be repeated and multiplied as many times as there are writers who sum up the cases.

Of the three parts of the duodenum in which primary carcinoma has been found, the weight of evidence is in favor of the second part being more frequently involved than the other portions. We must bear in mind in this connection that the *papilla Vateri* is situated in the middle part of the duodenum, that primary carcinoma of the common bile-duct at the ampulla, while uncommon, still occurs, and may give rise to an extension into the duodenum by contiguity. Unless careful examination of the structures involved is made, it would not be easy to say in what organ the tumor was primary. In this connection it might be well to point out that Rolleston[17] has shown that most of the so-called cases of carcinomata of the ampulla of Vater originate in the *termination* of the common bile-duct. One must differentiate between cancer of the termination of the common bile-duct, of the ampulla of Vater, and primary carcinoma attacking the mucous membrane covering the duodenal surface of the *papilla Vateri*, the last being a primary duodenal cancer, the former being much more common and coming under the classification of primary carcinoma of the biliary passages. Of the carcinomata of the middle portion of the duodenum, these circumpapillary carcinoma are the most frequent, and are especially prone to produce infections of the biliary ducts, as infective suppurative cholangitis and intrahepatic abscesses.

We should likewise exclude, in considering this topic, extension of carcinoma into the duodenum from other contiguous organs. Cases of carcinoma of the duodenum have been described as extending from the cæcum, ascending colon, transverse colon, the liver, the head of the pancreas, the gall-bladder, and the stomach.

Whittier[15] gives the location of the growth in 12 of the 13 cases he describes. The first and second portion of the duodenum was involved once, the second portion in 9 cases, the third portion once, and in 1 case the carcinomatous mass invaded the entire length of the duodenum.

In Pic's[16] 8 cases the location is given in 7, as follows: upper part of duodenum in 2, middle part in 4, and conjoined middle and lower portion in 1.

From Perry and Shaw's[2] report we gather that of 13 primary duodenal carcinomata 5 occurred in the upper part of the duodenum, 6 in the middle, and 1 in the lower part; the thirteenth case involved the entire length of the duodenum. It is curious to note here that in no case did the carcinoma extend through the pyloric ring into the stomach, a corollary to the fact brought out by Cuneo and Lucène[1] that pyloric carcinomata do not, as a rule, extend through the valve into the duodenum.

In 41 cases collected by Rolleston,[18] which probably include many if not all the cases of Perry and Shaw[2] and some of Nattan-Larrier's,[19] the first part was affected alone in 8, and together with the second part in 5 more; the second part was involved alone in 24 cases, and together with the first part in 5 as just stated, and the third part in 4. The third part is, therefore, the most infrequent as the seat of primary carcinoma. In this connection mention should be made of a very unusual case reported by Pye-Smith[20] of two distinct and separate carcinomata of the duodenum in one subject, the upper one involving the duodenum just beyond the pyloric sphincter, the other, the larger, occurring three inches lower down.

The Fenwicks[3] in their monograph on *Cancers of the Stomach and Duodenum* collected 51 cases of duodenal carcinoma, most probably including Whittier's, Pic's, some of Perry and Shaw's, Nattan-Larrier's, and Rolleston's cases, and found the following distribution: the upper third of the duodenum was involved in 11 cases, or in 21.5 per cent.; the middle third in 29, or in 57 per cent.; the lower third in 7, or in 13.5 per cent. In addition 8 of the cases involved the whole or the greater portion of the duodenum.

Varieties. In the great majority of the cases intestinal carcinomata are primary, very rarely are they metastatic. I have not come across the record of a single case of duodenal carcinoma which was metastatic in origin.

It is only within comparatively recent years that carcinomata were differentiated by histological differences. Early records of

duodenal carcinoma describe and differentiate them on the basis of their external appearances; thus the writers speak of them as soft or hard, fungoid or encephaloid, nodular or polypoid, and so on.

Regarding them from a histological point of view, the very large majority of duodenal carcinomata are of the cylindrical-celled variety, and show a glandular type, the so-called adenocarcinomata. A few cases have been reported of spheroidal-celled carcinomata, and their presence might raise the question as to whether such duodenal carcinomata were not extensions from the ampulla, from the *ductus Wirsungii*, or from the pancreas. According to the proportion of stroma to cells we have, on the one hand, when the stroma is abundant and the cells relatively few, the scirrhus form, and when the cells are in predominance and the stroma small in amount the medullary form. Both forms obtain in the cases reported. When the cells of the cylindrical-celled carcinomata of the duodenum undergo so-called mucoid or colloid degeneration they give rise to the gelatinous or colloid carcinoma of the duodenum. All forms are subject to retrogressive or necrotic change, whereupon softening and ulceration occur; in fact, these changes are common in duodenal carcinomata, and especially in those surrounding the *papilla Vateri*, and add to the disease picture a superimposed suppurative infection of the biliary passages and ducts or an abscess of the liver, as previously mentioned.

The tendency of growth is in an annular direction, more from the mucosa toward the lumen than into the underlying tissues of the mucosa, with the result that a more or less complete stricture of the duodenum occurs. Above the stricture dilatation takes place. Sometimes the stricture assumes a funnel shape. The spheroidal-celled variety grows more as a flat excresence with overhanging edges, and shows a greater tendency to ulcerate. The dilatation of the duodenum above the stricture may be very great, the walls of the dilated portion become thickened from hypertrophy of the muscular coat, and the mucous membrane shows the changes of a chronic catarrhal inflammation with superficial ulcerations.

Metastases are uncommon and, when they do occur, show themselves very late in the disease. Neighboring lymph nodes, it is said, are not often involved and likewise only toward the end of the disease.

Sex. Males form the preponderating majority of the victims of duodenal carcinoma. All of Whittier's[15] 13 cases were males; of Pic's[16] 8 cases, 3 were females. In the 43 cases tabulated by Rolleston[18] 33 of the patients were males and 10 were females.

Age. Victims of carcinoma of the duodenum are usually a little beyond the middle period of life. There seems to be a tendency for carcinoma to attack the small intestines a little earlier in life than does carcinoma of the other organs. The average age at which carcinoma of the duodenum occurs seems to be fifty-two years. Of

Whittier's[15] cases the youngest was seventeen years, two were eighteen years, and the oldest eighty-four; of Rolleston's[18] tabulated cases, 7 were seventy years or older, the youngest was twenty-seven, and the oldest was eighty.

Duration. The Fenwicks[3] place the average duration of life of the individual attacked with duodenal carcinoma as seven months, the extremes in their review of the cases collected being three months and eighteen months.

Symptoms. There is no doubt that there is a great difficulty in recognizing the disease during life. In fact, it is almost impossible to diagnose with certainty the disease when it attacks the upper portion of the duodenum, for then its symptoms are almost identical with those of pyloric carcinoma.

The symptoms will depend upon the site of the growth and its relation to the papilla of Vater; therefore, the symptomatology had best be given separately of the suprapapillary cases and of the infrapapillary ones. The cases of the juxtapapillary or circumpapillary variety present the picture of more or less complete obstruction of the common bile-duct, obstinate jaundice, cholæmia, and sometimes that of suppurative inflammation of the bile-ducts and multiple abscess of the liver. Their diagnosis, excepting as to probability, cannot be made, because their symptomatology does not sufficiently differ from carcinoma of the common duct, from carcinoma of the head of the pancreas, or from carcinoma of the ampulla of Vater. There occasionally occur rare exceptions to the rule of obstinate jaundice in the juxtapapillary or circumpapillary carcinomata, in which the jaundice may vary in intensity from day to day, and even entirely disappear for a time to recur shortly after. This is due to the fact that while the flow of bile is greatly interfered with it may not be completely blocked, and with the biliary *vis a tergo* increasing with the increasing pressure, the bile is finally forced through the obstructed opening of the papilla, or it may be that ulceration and breaking down of the growth may give rise to a reopening of obstructed channel. This seemed to be the case in a patient of mine,[21] who entered my wards at Mount Sinai Hospital on April 6, 1902, whose case was recorded by me in the *Mount Sinai Hospital Reports*, 1903, vol. iii. p. 49. In this case there was a carcinomatous growth lying at and around but not inside the papilla of Vater; it was annular, 8 cm. in diameter. The opening in the papilla was not entirely obstructed, but the orifice was overlapped by the growth; the pancreatic duct was much dilated and opened directly into the duodenum ½ cm. below the opening of the papilla of Vater, instead of joining with the common bile duct, which is the rule, to form the ampulla.

There was a complete obstruction of the orifice of the pancreatic duct by the growth, which proved to be an infected adenocarcinoma.

In all varieties the most pronounced symptoms are gastric, and similar to those of pyloric carcinoma, such as loss of appetite, eructations, nausea and vomiting, signs of increasing starvation, with its accompanying loss of strength and loss of weight; there are also abdominal pain and increasing cachexia. The pain is for the most part in the right hypochondrium, often in the epigastrium, and occasionally extends over the entire upper abdomen.

A tumor is often palpable in all varieties, though just as often one is not to be felt. When it is palpable it is situated in the right hypochondrium near the middle line of the body. It is slightly movable when the carcinoma is in the horizontal superior part of the duodenum; immovable when it occurs in the descending and in the inferior horizontal part, owing to the fixed connection of the latter two parts to the posterior abdominal wall.

Constipation, while it exists for the most part, is not a marked feature of the disease. It may be entirely absent or it may alternate with diarrhœa.

The abdomen is, as a rule, flat and even at times retracted or sunken.

The urine is diminished, the amount of chlorides diminished and occasionally entirely absent, and indican is often present in large but varying quantity.

The vomitus is very large, sometimes as much as seventy to eighty ounces, as one would expect to find in interference with gastric motility. Sometimes there is hæmatemesis, or vomiting of blood changed by the duodenal and gastric secretions—coffee-ground vomit. Persistent vomiting of bile is the distinguishing feature of carcinomata situated below the papilla Vateri. In all varieties the vomiting is recurrent.

Juxtapyloric or Suprapapillary Carcinoma of the Duodenum has all the subjective symptoms of the other forms. It has neither subjectively nor objectively any localizing signs which would suggest a prompt, even a probable diagnosis. Its chief subjective symptoms indicate a severe disturbance of gastric motility.

The objective signs are more important; the earliest is a tumor, more or less tender to the touch, painful, even independent of pressure. The tumor appears in the right hypochondrium near the median line; it is only slightly movable, if movable at all. Owing to the tendency of the growth to encircle the bowel and to produce a stricture, dilatation of the duodenum and the stomach result. The signs of gastrectasis develop, and gastrosuccorrhœa, with vomiting of large quantities of fluids, supervenes.

A tumor is not always palpable, and the signs of interference of gastric motility suggest most often the diagnosis of pyloric stricture or neoplasm.

The physical examination of the stomach contents will throw no light on these cases, although it is stated that the presence of free

hydrochloric acid in a case showing the signs of a pyloric carcinoma might suggest a diagnosis of juxtapyloric carcinoma of the duodenum. Boas observed a case in which the presence of free hydrochloric acid was demonstrated from the contents of a much distended stomach, and in which, owing to the absence of a palpable tumor, a diagnosis of benign stenosis of the pylorus was made; a laparotomy disclosed a neoplasm in the first portion of the duodenum. Boas[22] says we must not lay too much stress upon the results of chemical examinations, since free hydrochloric acid is often present for a long time in carcinoma of the pylorus, and, on account of the stagnation which results from proximity to the stomach, it may be absent and lactic acid present in duodenal carcinoma.

Czygan[23] called attention not long ago to the presence of splashing sounds between the tumor and free border of the ribs, and attributed them to the contents of a much-dilated duodenum. On removing the contents of the stomach the sounds disappeared, to reappear when that viscus was again filled. He insists that this sign is an important aid in arriving at a diagnosis.

Circumpapillary Carcinoma of the Duodenum. As we have shown, the descending portion is the most frequent site for carcinoma to affect the duodenum. When situated above the papilla its symptoms are similar to the juxtapyloric cases; when it involves the papilla it necessarily causes an obstruction to the flow of bile and jaundice develops. Jaundice is, therefore, the prominent sign. The jaundice is usually permanent, though in a few cases it has been absent entirely, the bile-duct not being obstructed; it has been intermittent or it has varied in intensity from day to day in still other cases. The subjective symptoms are indefinite and in themselves are of very little service in suggesting a diagnosis.

The objective symptoms are similar to the other forms of duodenal carcinoma plus the jaundice. A tumor is rarely felt, and in the cases in which a tumor could be palpated it was fixed and immovable in the right hypochondrium.

Jaundice comes suddenly and without pain, though in my case sharp pains preceded the development of jaundice, resembling an attack of cholelithiasis. Should signs of sepsis and tenderness over the liver follow, showing an infective process in the bile-ducts, one should bear in mind that such sequelæ may follow an ulcerating infected carcinoma of the duodenal papilla as well as an infection of the biliary passages due to a stone. If added to these symptoms obstinate vomiting, melæna, cachexia, and rapid loss of weight appear, a suspicion of juxtapapillary duodenal cancer might be formed. However, an absolute differentiation from carcinoma of the head of the pancreas is beyond clinical methods.

Infrapapillary, Juxtajejunal or Prejejunal Carcinoma of the Duodenum forms the smallest number of duodenal carcinomata, but comprises the cases in which occasionally a diagnosis

is possible. The diagnostic feature is contained in the vomit. Leichtenstern was the first to call attention to persistent vomiting of bile as the distinguishing feature of infrapapillary carcinoma. Pic[16] says Chomel[24] had previously, in 1852, called attention to this point. There is no doubt that in cases of duodenal stricture biliary vomiting is a marked feature. The stomach contents, even when there is no vomiting, or before vomiting occurs, will show the presence of bile.

For the same reason that bile is regurgitated into the stomach, the pancreatic secretion finds its way into that viscus. Should an examination of the contents of the stomach demonstrate the presence of the proteolytic ferment, trypsin, a diagnosis of obstruction below the biliary papilla may safely be made; when the other signs denoting a malignant disease are present a diagnosis of infrapapillary carcinoma of the duodenum would be justifiable. One must bear in mind, however, that the permanent presence of bile in the stomach contents alone is not sufficient to justify a diagnosis of prejejunal stricture, because in cases of gastrobiliary fistula bile is likewise to be found in the stomach. There must be associated the signs of lost gastric motility, the presence of trypsin, and the usual signs indicating malignant disease to justify the diagnosis of infrapapillary stricture due to malignant neoplasm.

Treatment. For the cure of these conditions therapeusis is of no avail. Whatever means we possess, whether medical or surgical, are merely palliative. Yet in surgical interference it would be well to bear in mind that in carcinoma of the first portion of the gut, if the technical difficulties be not too great (that is a question the surgeons must decide) a resection of the pylorus and affected portion of the duodenum might give some promise of a cure, because carcinoma of that portion very rarely extends beyond the pylorus, metastases appear only very late in the disease, and the neighboring lymph nodes are involved likewise very late. For carcinoma resulting in stricture of the other portions a gastroenterostomy may prolong life for some time. What hope of success would follow excision of the third portion of the duodenum when it is the seat of disease remains to be seen.

Thus far the only operation suggested as giving temporary relief has been a gastroenterostomy.

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PSEUDOLEUKÆMIA GASTROINTESTINALIS.

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Pseudoleukæmia, in which the lymphatic apparatus of the gastrointestinal tract is the seat of the principal lesions, has been rarely reported. In a somewhat extended review of the literature of pseudoleukæmia, under its various synonyms, with the view of

determining the frequency and extent of the lesions in this location, 238 cases have been found which came to autopsy. In 204 of these cases the gastrointestinal tract was recorded as normal, or was not mentioned, and therefore was probably not greatly, if at all, affected. Of the remaining 34 cases, 1 in 7 of the entire number, conditions varying from slight swellings of the mucous membrane and lymph follicles to extensive hyperplasia of the lymphoid tissue of the whole alimentary tract were found. In 15 cases the condition was confined to the intestines, while the stomach was affected seven times. In the remaining 13 cases both stomach and intestines were extensively infiltrated. In but 7 did the condition approach that found in the case we have to report.

Murchison, writing in the *Transactions of the Pathological Society of London* as early as 1869, recognized these peculiar conditions, and under the name of lymphadenoma presented a case which was in all probability lymphosarcoma, and which he reported as differing from any which he had met with or seen described, although Briquet, thirty years earlier, had described one of the most striking cases on record, which was also beautifully illustrated in Cruveilhier's *Atlas*. In 1884 Carrington reported a similar case, and considered the condition one of very great rarity, having found in the records of the Pathological Society and other sources but four cases resembling his, including Murchison's case. Again, in 1889 Pitt described these four and an additional one which had come under his own observation. Hadden reported his case as very unusual, having seen no other case in which the intestines were affected in "lymphosarcoma." Rolleston classified his case with Pitt's. In an extensive report in 1897 by Schlesinger on sarcoma of the stomach was reported a case as *pseudoleukœmia intestinalis*, and this case is also included in a series of four cases recently reported by Stoerk, three of which he had personally observed, and to which he gives the name of "pseudoleukæmia intestinalis or lymphosarcoma of the stomach." Seven cases presenting the most extensive gastrointestinal lesions have been selected and arranged chronologically in the following series:

Case I. (Briquet, 1838).—Male, aged forty-one years, with a clinical history of swelling of the testicles, inguinal region, and neck. Apparently the beginning was an inflammation in the mouth. This case is illustrated in Cruveilhier's *Atlas* (1839). The following findings were recorded: Mucous membrane of the mouth pale; at the base of the tongue the lymph follicles were greatly enlarged, and the tonsils were double their normal size. Trachea, larynx, and œsophagus normal. The stomach was of normal size, but its mucous membrane, which was pale throughout, was thrown into heavy, sinuous folds like cerebral convolutions, these folds terminating a short distance from the pyloric orifice; the other membranes of the stomach were normal. The mucous membrane

of the small intestine was gray and of normal consistence, but the surface was covered with a great number of polypoid growths, single and confluent. These were enlarged lymph follicles. These growths differed in appearance, some forming flat patches, while others were pea-sized and polypoid in form. In the upper part of the small intestine these growths were numerous, and in the lower half they were of a smaller size, but still more numerous. The Peyer patches were also enlarged and swollen near the ileocæcal valve, which itself was greatly enlarged, purple in color, and covered with miliary follicles. In the large intestine the follicles were very numerous, as large as the point of the little finger, polypoid and sessile, the mucous membrane being normal. The vermiform appendix was as thick as the thumb, and consisted of large follicles. The muscular and serous coats of the intestinal tract were normal. The lymphatic glands of the abdomen were greatly enlarged, as also were the spleen and liver. The kidneys and bladder were normal, and the prostate was greatly enlarged. No examination of the blood was made.

Case II. (Carrington, 1884).—A woman, aged fifty-five years, with enlarged cervical glands and a history of wasting for six months, without abdominal symptoms. At autopsy the cervical glands were found large and fleshy, as also were the mediastinal glands and the mesenteric glands. A large mass of glands pushed up the root of the mesentery and surrounded the pancreas. All the lymph glands were enlarged, especially in the portal fissure and the groin. The peritoneum was healthy. The stomach was studded over its mucous surface with very numerous cream-colored, flattened tumors; these were of mixed size, and some a little ulcerated. "Many of them were more infiltrations of the wall than distinct tumors; many, again, not even infiltrations, but conversions of the actual texture into new material." The pylorus was invaded by the same cream-colored growth, and was thrown into loose folds thereby. The duodenum was practically healthy, but below this the mucous membrane began to show disease. The valvulæ conniventes, here and there, first became swollen and firmer than natural, then polypoid and creamy. Sometimes a smaller or larger flattened swelling of the valvulæ occurred, with a little ulceration in the centre. This condition extended throughout the small and large intestine, but was more marked in the latter. The solitary glands and Peyer's patches were enormously enlarged, so as to constitute cream-colored, fleshy plates upon the surface of the mucous membrane. A few inches above the ileocæcal valve one growth of this kind measured one and one-half inches in diameter and half an inch in thickness. There was enormous thickening of the mucous membrane covering the ileocæcal valve, forming a thick fold surrounding the valve, of about half a pound in weight, which distended the cavity of the cæcum. There was neither con-

traction nor dilatation of the bowel in any part. The spleen weighed forty-four ounces. On section it showed a diffuse soft growth throughout, modelled on the normal pattern and color, so that the surface seemed to show enormous Malpighian bodies. The liver was normal. The blood count showed 4,720,000 reds and 4.3 whites to 1000 reds.

Case III. (Hadden, 1887).—A man, aged fifty-four years, with abdominal tumor and great emaciation. At autopsy a large tumor was found in the abdomen, involving the mesenteric and retroperitoneal glands; the axillary, inguinal, cervical, and iliac glands were also affected. There was a solitary nodule of growth in the liver. The spleen was large, measuring 10 x 5 inches, and studded with dull-white nodules. Near the pyloric orifice of the stomach there was one small, raised nodule of growth about one-third of an inch in diameter, apparently arising in the submucosa. All the intestinal glands, solitary and agminated, from the duodenum to the rectum, were much enlarged, elevated, and firm. This enlargement was very marked in Peyer's patches, and in the ileum near the valve the masses were enormous. The growth was strictly limited to the glands, and there were no ulcerations. Microscopically the hyperplasia of round cells was found localized to the glands without invasion of the surrounding parts.

Case IV. (Pitt, 1889).—The patient, a male aged forty-eight years, had gradually emaciated during the nine months preceding his death, but there were no symptoms of abdominal disease noted until the autopsy. At the base of the tongue were found three lymphoid masses, and there was a marked hypertrophy of the tonsils; the glands at the bifurcation of the trachea were large and swollen. There were enormous masses of lymphoid overgrowth on the mucous wall of the stomach, forming large, sessile tumors. At the cardiac end, two inches from the œsophagus, were large masses, both sessile and polypoid, one of which was $2\frac{1}{2}$ x 2 x 1 inch in size. Others occurred as raised vermiform overgrowths ramifying over the surface, of the thickness of a little finger. Over the greater portion of the body of the stomach there was also less extensive lymphoid growth, occurring in small, raised, flat patches of varying sizes. On the larger curvature, one and one-half inches from the pylorus, was a flat mass of growth one and one-quarter inches across, with a cupping of the surface which also occurred to a less extent in several of the other growths. The growths were all creamy-white in color, very soft and succulent, and the largest masses were breaking down at their bases. The mucous membrane was not ulcerated. In the duodenum immediately below the pylorus were numerous raised lymphoid growths about one-third of an inch across, stained slaty black. The whole of the small intestine was dotted with many thousands of raised polypoid growths about the size of large peas, scattered singly about, and there were flat

plaques of growth in Peyer's patches, which were raised about one-sixth of an inch; many of these growths were superficially ulcerated. There were large masses of growth along the ileocæcal valve, and the orifice of the vermiform appendix was occupied by a pigmented polypoid mass the size of a large chestnut. In the colon there was no lymphoid overgrowth. The mesenteric glands were universally swollen and enlarged. The spleen weighed 25.5 ounces, soft, and showed a general hypertrophy of the Malpighian bodies. The liver and kidneys were normal. No blood count was made.

Case V. (Schlesinger, 1897).—In his study upon sarcoma of the stomach, Schlesinger reports a case diagnosed during life by a nodule taken from the rectum, showing histologically what was considered a lymphosarcoma. The spleen and lymph glands were enlarged. Death was from facial erysipelas. Autopsy was performed by Prof. Kolisko, who made the diagnosis of *pseudoleukæmia intestinalis*. The patient was a male, aged sixty-two years. The spleen was three times its normal size, firm and bloody, with the follicles enlarged to pea size. The mesenteric lymph glands of the ileum formed immense tumors, were marrow-like, soft, and white. The mucous membrane of the entire intestinal tract was pigmented gray, and from the pylorus to the ileocæcal valve was covered with flat infiltrations standing out in patches, also of marrow-like consistence. In the entire large intestine were patches and polypi corresponding to the solitary follicles. The mucous membrane of the appendix was a finger thick, and of the same soft nature. The stomach and pylorus had polypoid infiltrations and sinuous folds. The mucous membrane was also thickened in masses. All the other abdominal glands were enlarged and soft. The blood count showed 2,100,000 red corpuscles, hæmoglobin, 55 per cent., and "few leukocytes."

Case VI. (Herrick, 1898).—A male, aged fifty years, was in the Cook County Hospital one and one-half years with all the glands, especially the cervical glands, enlarged. Attacks of erysipelas were followed by decrease in the size of the swellings. Death from exhaustion and dyspnœa. Autopsy by Prof. Hektoen. Enormous tumor masses were found in the neck and mediastinum, causing pressure upon the œsophagus and trachea. The nares and pharynx were filled with nodules, and the tonsils met in the median line. Tumor masses infiltrated the lungs, and the spleen showed one, but there were none in the kidneys and liver. General enlargement of the lymphatic nodules, Peyer's patches, and solitary follicles of the entire alimentary tract. The cæcum was filled with hard, blackish nodules, and masses attached to the wall of the intestine, while the vermiform appendix was thicker than a man's thumb, its lumen being filled with hard nodules and its opening into the cæcum occluded. The œsophagus contained many enlarged follicles. The mucous membrane of the stomach was the seat of a

universal diffuse invasion with these soft, white nodules, especially in the fundus, where the mucous membrane was thrown into large folds. The lymph glands throughout the body were greatly enlarged, and the pancreas was embedded in a mass of them.

Case VII. (Stoerk, 1904).—A woman, aged fifty-seven years, with a history of diarrhœa alternating with constipation, bloody stools, great abdominal pain, and œdema. At autopsy the lymph follicles at the base of the tongue and the tonsils were considerably enlarged. Cervical, mesenteric, retroperitoneal, and inguinal glands were all enlarged, and on the cut surface showed a gray-white, homogeneous appearance. The spleen measured 16 x 10 x 4 cm., flabby, with enlarged Malpighian bodies. The stomach was greatly dilated, and showed a peculiar stiffness of the wall. On opening the stomach the mucosa showed a very great thickening of the folds, running lengthwise. These folds were eroded at the summit, and showed some ulceration. In many places between the folds of the mucosa were white nodules the size of a pea, with melanotic discoloration. The pylorus was involved in this condition, and the duodenum to a less extent; the folds were increased in size, and contained prominent lymph follicles. In the small intestine the same condition was present, and Peyer's patches were enlarged. In the large intestine the mucous membrane was very much thickened and covered with numerous enlarged, single, discolored follicles. Especially remarkable was the condition in the colon, decreasing from the cæcum toward the anus. The bone-marrow was deep red, soft, and moist. Microscopically a very slight infiltration of round cells was found in the kidney and liver. The blood count showed: lymphocytes, 41.2 per cent.; large mononuclears, 4.6 per cent.; eosinophiles, 1 per cent.; neutrophiles, 53.2 per cent., and a few myelocytes.

Rolleston and Latham report a case somewhat similar to that of Pitt's, with much hyperplasia in the stomach, but not in the intestine, and not well generalized in the lymph glands. However, the blood showed evidences of splenomyelogenous leukæmia, and, as the authors are in doubt as to its proper classification, it has seemed best not to include it in this series. There is much reason to believe, however, that this case is of the type that has sometimes been reported as an instance of pseudoleukæmia becoming transformed into leukæmia.

Case VIII.—On November 17, 1903, the following typical case of pseudoleukæmia gastrointestinalis was examined post-mortem at the Chicago Baptist Hospital: E. H., a minister, aged fifty-one years, was admitted to the service of Dr. J. P. Webster, to whom we are indebted for the privilege of reporting the history of the case, kindly furnished by the house physician, Dr. Adams. He was a strong, athletically inclined man, who had been well until the preceding winter, when he complained of "feeling as if he were going to be

sick." This feeling persisted through the spring. In April he caught cold, and was confined to his bed for six weeks with a severe bronchitis, from which he was not expected to recover; he had high fever and night-sweats. He gradually recovered from this illness, but never again became perfectly well. He became anæmic, and in October began to have night-sweats. Fresh air and dietetic treatment had little beneficial effect. Massage was tried, first of the limbs, and then of the stomach and bowels, on account of "poor digestion." Vigorous massage over the stomach caused a feeling of "goneness." In September he took a trip through Iowa, during which his health failed rapidly. He was told that he had kidney trouble, and took some proprietary treatment for it, but this disturbed his stomach so much that he was forced to give it up. At this time he complained of "grabbing pains" in the region of the stomach, and jerking of the limbs. At this time urinalysis was made, and nothing abnormal found. On admission to the hospital for an exploratory laparotomy, which had been recommended, examination revealed the following condition: The patient was anæmic, temperature normal, pulse from 90 to 100. The lungs showed signs of a slight bronchitis, and the heart was negative. Abdomen very tense and tympanitic, and tender on deep pressure over the stomach. With some difficulty a tumor mass about the size of a man's fist was outlined by percussion and palpation, corresponding in position to the region of the pylorus. The lymph glands were enlarged all over the body, varying from pea to almond-size.

Urinalysis was negative. The diagnosis that was made lay between carcinoma of the pylorus and tuberculous peritonitis without effusion.

On opening the abdomen for the purpose of laparotomy the stomach was found greatly dilated, and its wall thickened from pylorus to cardia; the duodenum also seemed to be thickened. Gastroenterostomy was performed, uniting the upper part of the jejunum to the lower posterior part of the stomach by means of a Frank button. When the stomach was opened the organ did not collapse, because of the diffuse thickening of the walls, and the rugæ were found to be as thick as the finger. A piece of the mucous membrane and one of the enlarged mesenteric glands were removed for microscopic examination. As was to be expected, the diseased organ did not react well to the operative procedure; leakage occurred about the button, and death occurred eleven days later from peritonitis. Unfortunately, at no time during the patient's illness was a blood examination made.

The tissues removed at the operation were sent to the Pathological Laboratory of the University, and the diagnosis of "pseudoleukæmia, with hyperplasia of the lymphatic apparatus of the stomach" made on the histological findings.

Autopsy was performed five hours after death, and the report upon the findings is as follows:

Anatomical Diagnosis. Pseudoleukæmia; general lymphadenoid hyperplasia, particularly of the alimentary tract and peripancreatic glands, with resulting enlargement of stomach and appendix; diffuse acute suppurative peritonitis; recent laparotomy wound, infected; anastomosis of stomach and duodenum by suture and Frank button; hyperplasia and hyperæmia of red bone-marrow; hyperplasia of Malpighian bodies of spleen; parenchymatous enlargement of liver and kidney, with lymphoid infiltration; sclerosis of coronary arteries (minimum degree); apical, fibrous pleuritis; hypostatic congestion, bronchopneumonia, and œdema of lungs; fibrous perisplenitis.

External Appearances. Body of a tall, slender, poorly nourished man, 175 cm. in length. Body not entirely cold, having been dead but five hours. Rigor mortis present. Sclera white. The skin is pale. In the median line of the abdomen is a long operative wound (gaping), 18 cm. long. The floor and walls show a purulent fibrin. The floor of the wound is formed by the parietal peritoneum and by the intestine bulging through the peritoneum. The muscle on the sides of the wound is pale and wax-like.

Abdominal Cavity. The intestines are everywhere matted together by easily torn, fibrinous adhesions. The cavity contains about one litre of thin, yellow, opaque, purulent fluid. Between the stomach and the diaphragm on the left side is a collection of thick, yellow, purulent material. The stomach is distended and also the intestines to a moderate degree. The peritoneum is covered with a thin layer of fibrin. Between the folds of the intestines drops of pus are found. There are no adhesions between the liver and the diaphragm, but a few about the spleen. Every other part of the peritoneal cavity is obliterated by adhesions.

Pleural Cavity. Lungs meet in the median line. On the left side are a few fibrinous adhesions at the apex; pleura smooth. No other changes.

Pericardial Cavity. Pericardium smooth and shining, free from adhesions. The cavity contains about 50 c.c. of clear, serous fluid.

Thyroid and Thymus. The fat at the site of the thymus shows evidence of some lymphatic tissue.

Heart, Aorta, and Vessels. The heart is of normal size. The coronary arteries are tortuous. There is a considerable amount of fat. The ventricles contain large, soft, pale clots. The anterior coronary artery has slight patches of thickening. The aortic and pulmonic valves show no change. The myocardium is firm and of normal color. The tricuspid orifice admits five, the mitral orifice admits three finger-tips. The mitral and tricuspid valves show no change. The foramen ovale is closed; the endocardium is normal.

Lungs. The right lung has few adhesions between the lobes. The posterior is heavier than the anterior and darker. At the apex are a few hard, fibrous nodules. The upper lobes contain considerable fluid. The dark parts of the lower lobe crepitate but little and contain a bloody, frothy fluid. The left lung is the same as the right, except that the dark area is smaller. At the hilum are also small, hard glands.

Liver. The liver is enlarged, measures 28 x 21.5 x 17 x 11 x 6 cm., and weighs 2470 grams. The enlargement is diffuse. The external surface is roughened, as if each lobule is enlarged. Beneath the

FIG. 1.

Lymphoid hyperplasia of the stomach. The stomach is shown in this illustration inverted, to show the enormous thickening of the rugæ, and on account of the thickness of the walls is thereby made somewhat smaller than when in its natural condition. The stomach wall weighed 1300 grams—nearly as much as a normal liver.

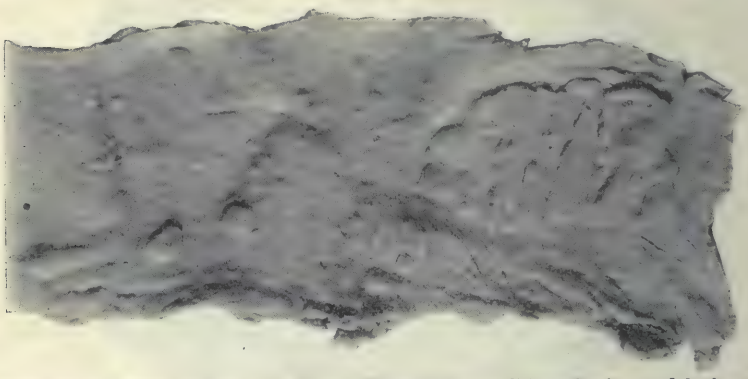
capsule there are numerous pale, slightly elevated areas, that do not penetrate the liver substance. The consistence is slightly increased. Individual lobules are enlarged and much lighter than normal, except in the centre.

Spleen. This is slightly enlarged, weighs 160 grams, and is of normal consistence. The cut surface shows the Malpighian bodies much enlarged and prominent. Pulp has but little blood, and is not softened.

Pancreas. The pancreas is of normal size and shows no gross changes, although a string of greatly enlarged glands lies along the upper border.

Gastrointestinal Tract. The stomach is enormously enlarged, and weighs 1350 grams when empty. Along the attachment of the omentum are numerous pea-sized lymph glands. When cut open it does not collapse, because the walls are much thickened. This thickening is fleshy, diffuse, yet nodular in places, and the thickness of the opposed walls together is from 4 to 5 cm. The rugæ are much swollen, and in places form tumor-like masses about 2 to 4 cm. thick. These are soft, being about the consistence of the large soft lymph glands. The thickening involves every part of the stomach, and is greatest about the pylorus. A Frank button is found in a sutured opening between the duodenum and stomach. The entire length of the stomach along its greater curvature when collapsed is 57 cm.; its straight length, 33 cm.; width, collapsed, 13.5 cm.; thickness, 5 cm. by external measurement. There is no ulceration or other change in the mucous surface. The duodenum

FIG. 2.



Hyperplasia of Peyer's patches and solitary follicles of the small intestine in pseudoleukæmia gastrointestinalis.

is not greatly thickened. The cæcum shows great thickening of the wall, which is reddish, and resembles the stomach, the greatest thickening being at the beginning of the appendix, where there is a mass 4 cm. in diameter. The solitary follicles and Peyer's patches are thickened, raised, pigmented, and slate-colored. The change is more marked toward the lower end. The whole intestine weighs 1500 grams, and shows similar thickening of the lymph follicles. The lower end of the ileum shows Peyer's patches greatly enlarged, some measuring 7 x 3 cm. and being 8 mm. thick. The solitary follicles are slate-colored. The mucosa is a little thicker than normal. Farther up the enlargement of solitary follicles decreases, although Peyer's patches are all enlarged.

The appendix is solid in all its extent. It is 8 cm. long, adherent by its tip. It is larger toward the tip, where its circumference is about 57 mm. It has a mesentery about one-half its length, in

which are numerous lymph glands 5 mm. in diameter. The enlargement is solid and uniform, the consistence that of the normal appendix. The lumen seems open. The mesocolon is swollen and reddened. The mesentery is very friable.

Adrenals are of normal size. The cortex seems thicker than normal, and is pale and solid.

Kidneys. Their combined weight is 400 grams. The right kidney is a little enlarged. The consistence is normal. The cortex is thickened, measuring 7 x 10 mm. It is generally pale, and the cortical markings are obscure. The capsule strips easily. The left kidney is the same as the right.

FIG. 3.

Hyperplasia of the lymphoid tissues of the cæcum, appendix, and lower end of the ileum. The orifice of the canal of the appendix can be seen in the summit of a tumor-like mass in the cæcum. In the ileum is seen an enlarged Peyer's patch.

Urinary Tract. The urinary bladder is not thickened. The prostate is not enlarged.

Generative Tract. The testicles appear normal.

Lymph Glands. The suboccipital glands are not palpable. The posterior cervical glands are 0.5 x 1 cm. in size. The submaxillary glands are twice the normal size. The glands beneath the sternocleidomastoid and about the clavicle are not palpable. The axillary glands are much enlarged on both sides, about the size of cherries; those at the elbow are not palpable. The inguinal and femoral glands on both sides measure from 1 to 1.5 cm. in diameter. The glands at the hilum of the lung are large, soft, and anthracotic. In the posterior mediastinum is a group of glands measuring altogether 1 cm. by 5 cm. None of them is calcified or caseous. At

the attachment of the stomach to its ligaments are many enlarged, pale glands. The peripancreatic glands are enormously enlarged, the largest being 35 mm. long, very soft, pale, with small hemorrhagic spots. The retroperitoneal lymph glands are much enlarged. At the hilum of the liver the lymph glands are enlarged, soft, and pale. Lymph glands of the anterior mediastinum are not prominent; those of the neck and behind the clavicle are enlarged, flesh-like in consistence, pinkish in color. Some are deep red. The mesenteric lymph glands are enlarged, averaging about twice the normal size. The mesentery and omentum are everywhere studded with lymph glands. In the mesocolon are many dark-red lymph glands.

Skeleton. No changes except that the marrow of the clavicle shows a few yellow areas, the rest being bright red. Femurs could not be examined. Marrow of sternum very abundant, bright red, and pulpy.

Histological Report. Mediastinal Gland (small, measures about 5 mm. in diameter). In the fatty tissue about the gland are a number of small islands of lymphoid tissue, not connected with the gland proper. The gland under low power presents a normal arrangement of its structures, but differs from normal in that both the lymph nodes and the sinuses are much enlarged. The capillaries are all considerably distended with blood. In the lymph nodes the germinal centres are not distinguishable. The cells of the nodes are of the usual small round type, but there are many more pale nuclei than usual; karyokinetic figures are not abundant, although occasionally seen. The only unusual cell type in the lymph nodes is a frequently found form that consists merely of a large ring, taking the nuclear stain at its periphery only, and in a very few granules found within its circumference. Occasional similar types of an elongated form can be seen. These seem to be hydropic nuclei of germinal cells. The sinuses are crowded with a great variety of cells, of which the most abundant are large endothelial cells, lymphoid cells, and plasma cells. Polymorphonuclear leukocytes are present, but in small numbers. Eosinophiles are occasionally found, generally just outside a lymph node, although they do occur free in the sinuses; a few of them have nuclei resembling those of the plasma cell. The most striking features of the sinuses is the great number of plasma cells. In some fields they form by far the majority of the cells present, and in the sinuses, as a whole, are equal in number to either the lymphoid or endothelial cells. They often tend to group themselves together in nodules as large as the field of a $\frac{1}{12}$ inch objective, with but few other cells among them. A few mast-cells are found, much less abundant than the eosinophiles. There are not a few red corpuscles also present in the sinuses. Phagocytosis is not a prominent feature, yet large endothelial cells are frequently found containing various other cells,

especially red corpuscles, and lymphocytes, and frequently plasma cells. No giant cells were found.

Pancreatic Lymph Gland (largest gland in the body). Here the ordinary structure of a lymph gland is entirely lost, it being impossible to recognize any of the normal anatomical structures. The gland consists merely of a mass of cells of various sorts, in differing proportions in different areas, held together rather loosely. The bloodvessels are not numerous, and the lymph sinuses cannot be recognized. Occasionally small areas of necrosis are found, irregularly defined, and often containing many normal cells. Standing out prominently are small groups of very deeply staining nuclei located particularly at the periphery of the gland, but not distributed regularly. The predominant cell in this gland is one with a nucleus slightly larger than that of the ordinary lymphoid cell, usually round, but varying much in size and shape, the nucleus usually staining very deeply, but all degrees of staining are present, from nuclei nearly a solid black to those only staining at the periphery. These cells have very little cytoplasm, but occasionally have a double nucleus. Mitotic figures are abundant in them. They are distributed everywhere in the gland without any definite arrangement. In contradistinction to the small glands, plasma cells and eosinophiles are absent. Large phagocytic endothelial cells are abundant, and usually present abundantly in ill-defined areas, which probably represent the original sinuses of the glands. They are generally packed with cells, the most common of which have a single small nucleus, staining intensely in some, but in many the staining affinity for hæmatoxylin has been replaced by affinity for eosin. Red corpuscles are also often present in the phagocytes, and they are also quite numerous, lying free among the cells. All sorts of nuclear degeneration are present, and nuclear fragments, pyknotic and vacuolized nuclei are very abundant, as well as nuclei that have lost their affinity for basic stains. A very few cells contain yellow pigment granules. Polymorphonuclear leukocytes are very few in number.

Lymph Glands in General. Lymph glands of a size intermediary between these two, which represent extremes in this case, show changes corresponding to the relation in size to either extreme. The early changes seem to be chiefly a proliferation of lymphoid cells in the nodes, and of plasma cells in the medullary cords. Later the lymphoid cells overrun everything, and show at the same time both proliferative and retrogressive changes going on side by side, recalling the old distinction between leukæmia and pseudoleukæmia, in that in the latter "the gland cells proliferate but do not leave the glands." The plasma cells, and also the eosinophiles, disappear in the later stages. Giant cells of the type described by Reed are very scanty, not averaging more than one in a section, and are most numerous in the glands in intermediary stages.

Stomach. The great thickening of the wall is due to an enormous enlargement of the lymphatic structures of the stomach wall. Where a follicle normally existed is a mass of lymphoid tissue often 5 to 7 mm. in diameter, while between these nodes a diffuse proliferation of similar tissue has thickened the mucosa uniformly to a width of 3 to 5 mm. Occasional microscopic accumulation of lymphoid tissue is present between the layers of the muscularis, but the proliferation in every instance respects the connective and muscular layers of the stomach, never penetrating them to invade the deeper layers. There are, however, a few round cells and polymorphonuclear leukocytes between the muscle fibres. As the surface epithelium is not present in the specimens, it cannot be positively determined whether the lymphoid tissue has reached the surface or not, but the indications are that it seldom if ever passes beyond the basement membrane of the surface epithelium. There are no evidences of ulceration or infection. The structure of the proliferating tissue is quite the same as that of the lymph glands. Plasma cells and eosinophiles are abundant, particularly near the surface, while the central part of the new tissue is chiefly small round cells. Phagocytes are not abundant.

Intestines. A hyperplasia of all the lymphatic structures of the intestine is present, similar in all respects to that of the stomach. The growth respects always the surrounding tissues, and there is no ulceration. Not only are the solitary and agminated follicles enlarged, but small islands of lymphoid tissue seem to develop at frequent intervals. The chief difference from the stomach is that outside of the follicles there is not the diffuse lymphoid hyperplasia of the mucosa, so that the wall is not so universally thickened.

Œsophagus. Numerous areas of lymphoid tissue are found, particularly about the deeper glands, but there are none of any very great size.

Spleen. To the naked eye sections of spleen present a striking appearance, because of the deep stain of the Malpighian bodies in contrast with the pulp. Microscopically the changes are quite different from those in the lymph glands. The Malpighian bodies are generally larger than normal, and consist of two zones, a central mass of nuclei staining dark blue, and a peripheral zone of lighter staining, but more densely packed cells. The arteries within the Malpighian bodies are hyaline, and within the bodies are often present also masses of homogeneous material, arranged in bands, and staining intensely with eosin. This material is not found in all the bodies, and never in the pulp. The cells in the centre of the bodies are almost solely the deep staining mononuclear cells, which show neither mitosis nor degenerative changes. There is much increase in the amount of pulp. Red corpuscles are found in contact with the hyaline masses, but not elsewhere. The outer zone of the bodies consists of cells with elongated nuclei and a small

amount of cytoplasm; there are appearances that suggest that these cells are derived from the round cells. In this zone plasma cells are abundant. The pulp is very different from normal, consisting of broad bands of cells with considerable cytoplasm and little intercellular substance, forming a meshwork in the interstices of which red corpuscles are found. These bands seem to be formed by proliferation of the cells of the spleen sinuses of the endothelial type, although there are also very many plasma cells, and frequent eosinophiles and lymphoid cells. There seems to be much filling up of the spleen sinuses by these proliferated cells, which frequently contain granules of golden pigment, and occasionally red corpuscles and lymphoid cells. The total amount of blood in the spleen is small. By Van Gieson's stain there is no increase of material taking the red stain anywhere in the organ.

Thymus. This organ seems to have largely escaped the general lymphatic hyperplasia, for it contains no more lymphoid tissue than is often found in adults, although probably more than is usually found in men of the age of fifty-one. The largest nodes are the size of a pinhead, and consist almost solely of small lymphoid cells. The appearances indicate that the amount of lymphoid tissue is greater than it was at some previous time, but the lymphoid nodes are still few and far apart. No evidences of Hassell's corpuscles are found.

Other Viscera. In the *kidney* are numerous accumulations of lymphoid tissue, the largest not over 0.5 mm. in diameter, and located only in the cortex in the sections examined. These cells are of the lymphoid type almost exclusively; are arranged in illy defined groups, infiltrating between the renal tubules which seem to be destroyed when surrounded by the cells. Plasma cells and eosinophiles are absent from these areas. The *liver* is studded with lymphoid areas, which follow along the course of Glisson's capsule at all points; it is impossible to find a group of the vessels not surrounded by the new cells. The largest of these areas is the size of a liver lobule. No such areas are found in any part of the lobule except about the portal vessels. The cell masses do not tend to infiltrate between the liver columns as they do between the renal tubules, but rather push them aside *en masse*, for which reason, probably, the new cells are often elongated and irregular. Plasma cells and eosinophile cells are not found. In the *prostate* are many accumulations of lymphoid tissue, some 1 to 2 mm. in diameter, infiltrating extensively between the muscle fibres. There are some small accumulations in the *adrenal*, chiefly in the medulla about the large vessels, and a few are found about the vessels in the interstitial tissue of the *pancreas*. The *thyroid*, *testicle*, and, so far as examined, the *lungs* were free from lymphoid proliferation.

The Blood. As no examination had been made during life, smears were made from the heart's blood at autopsy, but for some

reason it was impossible to secure satisfactory stained preparations from these. It could merely be determined that there was no apparent increase in the number of leukocytes, and that of these more than the usual proportion were lymphocytes. Examination of the blood in the sections of the various organs made it seem that there was little more than the normal number of leukocytes in the blood. An attempt at a differential count was made by counting the leukocytes in the larger vessels in the capsule of the thyroid and the testicle in several sections; these organs were selected as offering less possibility of "dragging in" of cells by the knife, and as being most nearly normal of any of the organs. Vessels with thrombi or unusual collections of leukocytes were excluded. Only cells that were definitely either lymphocytes or polymorphonuclear leukocytes were counted, transitional and doubtful forms being excluded, and of 500 cells so counted 47 per cent. were polymorphonuclear and 53 per cent. lymphocytes. It must be borne in mind that death in this case was due to suppurative peritonitis, with terminal septicæmia.

Bacteriological Examination. Staphylococcus pyogenes aureus was obtained from the heart's blood and viscera, and was associated with B. coli in the peritoneal exudate.

Animal Inoculation. Five guinea-pigs were inoculated with 2 cm. each of thick emulsion of glands, taken from all parts of the body and ground up together. The pigs were inoculated intraperitoneally on November 17th. One died after four days with an acute pneumonic process. No peritoneal or other changes. One died on December 14th with a pneumonic condition, and showed no evidence of tuberculosis. However, one peripancreatic gland was 15 mm. in diameter, and contained a large amount of very thin pus, forming little more than a sac for the pus. This pus was stained for tubercle bacilli with negative results; likewise the wall of the abscess. Histologically it seemed a simple pus sac. After two months the three surviving guinea-pigs were killed, and found perfectly normal; no evidence of the injections of any kind; no tuberculosis, no lymph-gland enlargement.

Analysis. In all but one of these eight cases, including our own, the ages varied between forty and sixty, the average being a little over fifty. Murchison's case, which is included by some of the English writers, is almost certainly lymphosarcoma, and not pseudoleukæmia in the ordinary sense. Schlesinger's series of lymphosarcoma of the stomach shows the most frequent age of this closely allied condition as between twenty and thirty-five. There were six men and two women, which agrees with the greater frequency of pseudoleukæmia in men.

In every case there was greater or less general enlargement of the lymph glands throughout the body. In some the greatest increase was in the cervical glands; in others, especially in our case, in the

abdominal glands receiving the lymph from the involved portions of the alimentary tract.

Enlargement of the spleen is nearly constant, in the largest the weight being forty-four ounces. More characteristic is the constant enlargement of the Malpighian bodies, which was marked in all. The liver is less frequently enlarged, but in some of the cases is the seat of considerable lymphoid infiltration and enlargement, as in our case. The kidneys seem to be less often affected than the liver. In other words, the distribution of changes outside the gastrointestinal tract is not different from what may be found in any ordinary cases of pseudoleukæmia.

As for the alimentary tract itself, it is observed that the form taken by the hyperplasia varies somewhat with the location. 1. Immense, loose, sinuous folds, like cerebral convolutions, are found in the stomach. 2. Polypoid forms, those of pea-size almost countless in number, increasing to the size of chestnuts. 3. Extensive slightly raised patches corresponding to Peyer's patches. 4. These polypoid growths and patches are frequently pigmented a slaty black, and less frequently ulcerated. Outside of the infiltrations the mucous surface is usually normal, and the ulcerations are usually slight and superficial. The tissue increase is limited to the mucous and submucous coats, the muscularis not being invaded to any extent. An interesting fact is that in spite of the enormous thickenings the lumen of the bowel is not altered in size.

Stomach. In every case but one the mucous membrane of the stomach was thrown into great sinuous folds, ulcerated to a slight extent in three cases, but maintaining usually its normal external appearance. The immediate vicinity of the pylorus was not involved in some of the cases. Pitt remarks that it is not clear why the growth is so scanty at the pyloric end of the stomach, where, according to Watney, the lymphoid tissue is so abundant. The duodenum is least affected, having very few or no lesions.

The small intestine in every case presented small, pea-sized polypoid growths, and extensive pigmented, flat infiltrations of Peyer's patches. In the region of the ileocæcal valve and appendix the thickening in every case was enormous. Next to the duodenum the large intestine was least affected.

The clinical symptoms were very meagrely reported in most of the cases. They present the usual conditions of pseudoleukæmia, with rarely any symptoms to indicate that the gastrointestinal tract was involved, probably because there is no obstruction to the bowel and no ulceration of the surfaces. Stoerk's patient showed bloody stools, and in our case the history of digestive disturbances and the palpable tumor led to an exploratory laparotomy.

General Summary. The frequency with which the first or most extensive enlargement of the lymph glands in Hodgkin's disease has been observed in the cervical region has suggested to many the

possibility that the infectious agent, if such there be, might have entered *via* the tonsils, infected the cervical glands, and later become generalized throughout the body. Such a conception is supported by the cases of pseudoleukæmia discussed here, and particularly by the one we report. In this instance by far the most advanced manifestation of the disease was in the stomach, and next to the stomach the glands that receive its drainage. Although all the lymph glands were more or less enlarged, none compared with those about the stomach in size. Another peculiarity noted, in reviewing over two hundred autopsies in pseudoleukæmia as recorded in the literature, was that whereas in the universal enlargement of lymphatic tissue that of the alimentary canal usually participates little or not at all, yet when it does become involved to any extent it is likely to happen that it is then involved much more in proportion than any of the other lymphatic tissues. This recalls a similar peculiarity of many known infections, *i. e.*, that when they once have made headway with a certain sort of tissue they often tend to invade almost exclusively similar tissues in other parts of the body. This tendency to affect the gastrointestinal lymph apparatus, as seen in this particular group of cases of pseudoleukæmia, has seemed to warrant their collection and publication together as a subdivision of the general group of cases that presents the anatomical and symptom-complex of Hodgkin's disease, to call attention to their existence. Apparently this group in which the chief alterations are in the gastrointestinal tract is neither clinically nor etiologically different from the ordinary cases, and anatomically the difference lies solely in the distribution of the lesions.

Such cases stand particularly near the lymphosarcomas, and the confusion in nomenclature of pseudoleukæmia has added to the difficulty of distinction in many of the recorded cases. Murchison's case, according to his description, is an example of a real malignant tumor, a lymphosarcoma of the duodenum with involvement of the regional glands, yet it has been classified in the literature as pseudoleukæmia. Limiting the term lymphosarcoma to true malignant tumors, there can be no question of sarcoma in the cases we have under discussion, for they do not infiltrate, they attack only lymphoid tissue, and in doing so disobey all the laws of metastasis, and they possess particular histological features that are incompatible with sarcoma. Following up the changes in the lymph glands in our case in the order of extent of enlargement, it is readily determined that the growth is derived from the cells of the glands themselves, which multiply from certain anatomical locations in the glands, and pass through certain steps in their development, and that it is not a matter of growth from foci of cells entering the gland from without and assuming a certain fixed type, as would be the case with a metastatic growth. The best proof of all, perhaps, is the readiness with which the cases of lymphosarcoma of the

digestive tract can be separated from these forms of pseudoleukæmia by the anatomical findings reported, no matter under which of several names they may be found classified.

Tuberculosis as a cause of Hodgkin's disease has been thoroughly discussed of late with a negative verdict, although certain cases show that we may have clinically a symptom-complex not different from that of Hodgkin's disease, associated with universal tuberculous lymphadenitis. Our case may be added to the now fairly considerable number in which animal inoculation as well as microscopic examination has failed to demonstrate the presence of tubercle bacilli.

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THREE RECENT CASES OF CROUP DUE TO STAPHYLOCOCCUS AND REQUIRING TRACHEOTOMY.[1]

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Croup is a term which has by time and usage earned a permanent position in our medical vocabulary, and yet with the progressive development in modern pathology its meaning grows steadily more ambiguous. Heretofore such prefixes as "true," "pseudo," "membranous," etc., helped to designate the special form intended; for example, membranous croup meant laryngeotracheal diphtheria due to the Klebs-Loeffler bacillus. Billings in a bacteriological analysis of 286 cases of membranous laryngitis showed 80 per cent. to be due the Klebs-Loeffler bacillus and 20 per cent. to streptococci and diplococci. We also know that pseudomembranes may be induced by the local action of chemical and physical agents. Gould's dictionary defines "croup" as "a disease of the larynx and trachea of children, prominent symptoms of which are peculiar cough and difficulty in breathing; it is often accompanied by the development of a pseudomembranous deposit or exudate upon the parts." The latest authorities still differ as to the proper interpretation of various

[1] Read at the Cleveland Meeting of the Ohio State Medical Association, May 20, 1904.

prefixes placed before the term croup. Jonathan Wright, in his latest text on nose and throat diseases gives a special heading entitled "Acute Catarrhal Laryngitis in Children"; this title will best include the cases to be described in this paper. The clinical characteristics of acute laryngitis are familiar to every medical practitioner, and I shall proceed at once with three interesting cases which came under my observation last winter.

Case I.—A male babe, aged eleven months, was of fair build, and had always been well. On December 1st the mother had "aching in the bones," a chill, fever, sore throat, and enlargement of the cervical glands. The next day the older of her two children, aged three, took sick with the same symptoms. On the third day the babe was similarly affected, and drowsiness was especially noted. The mother was well in about ten days, but the children continued in their ailment, some days better, then again worse. After domestic remedies had been used for about two weeks, Dr. Vance was called, who pronounced the condition tonsillitis. He found the temperature ranging from 101° to 102°, and on several visits the same was normal. At the end of the third week the babe became "croupy," and the glandular swelling on the right side of the neck became larger and more diffuse, simulating a cellulitis. The next day the breathing was more labored and with a distinct stridor audible all over the room. The following night strangling spells caused much anxiety. The following morning the symptoms subsided, but the breathing was still labored. At noon I was called to make a bacteriological examination of the throat. I found moderate hyperæmia and swelling of the pharynx, but no membrane. The throat swabs showed microscopically the presence of a few saprophytic bacilli and a predominance of diplococci. Late in the afternoon the child had a temperature of 103°, weak and rapid pulse, pallor and cyanosis, and beginning coma. Tracheotomy had been advised the day before, but was refused. Consent now being given, the chances even with operation were very doubtful. Dr. Rind did a "high operation," and on opening the trachea nothing more than a slight congestion with small quantity of mucus exudate was seen. Swabbings taken from both larynx and trachea showed on subsequent examination pure cultures of a diplococcus. Probing toward the larynx, this was found occluded by intense swelling. Respiration gradually became rhythmic, and thirty minutes later the child was placed in bed quietly breathing through the tube. The color and pulse improved rapidly. From this time on a tabulated record was kept which showed for the following few days a temperature ranging from 101° to 104°; pulse, 135 to 140; respiration, 40 to 50. The cellulitis on the right side of the neck subsided within the next two days, but the swelling in the larynx continued for five days, whereupon the breathing was re-established through the natural channel, and the tube was left out alto-

gether. Strict asepsis was observed throughout, but considerable suppuration occurred in the wound, due, probably, to the organism found in the trachea. The wound healed by granulation in two weeks. The child made a perfect recovery, and is well to-day. In passing it may be mentioned that the nurse who waited on the mother during her illness was taken with sore throat and glandular enlargement the week following her departure; moreover, the daughter of the nurse was similarly affected.

Case II.—A female, aged four years, quite plump, had always been well excepting throat trouble during the winter months. About four weeks before the present trouble the whole family, including father, mother, and two children, had mild sore throats. Dr. Rind was called several times to see patient aged four, because she seemed to be worse than the others. He found nothing significant, and made a diagnosis of tonsillitis. On January 7, about three weeks from the onset, the patient had "croup" symptoms. Dr. Rind being ill, Dr. Vance was called, who found a temperature of 101°, pulse 130, high falsetto voice, and respiratory stridor. On the same day I was called to make a throat examination and found moderate congestion and swelling of the larynx, but no membrane. The throat swabs showed a few non-characteristic bacilli and a predominance of diplococci. It was evident from close clinical observation that the obstruction was both mechanical and spasmodic. During the afternoon the condition grew progressively worse, and 5000 units of antitoxin (Mulford's) was given as an extra precaution. About two hours after this the child had its worst strangling spell, and the nurse thought it was dead. I arrived fifteen minutes later and found the child recovered from the attack, but in general the condition was worse than before. In the evening four physicians in consultation decided that operation should be done. The temperature was now 102°, and pulse 130. At 9 p.m. Dr. Rind opened the trachea high up, which was difficult, owing to the excessive adipose tissue and engorged veins. When the trachea was incised no air entered, and we feared membrane. However, on closer inspection a diaphragm was visible, extending obliquely across the lumen of the trachea, and on puncturing this air entered with a gush. This diaphragm must have been either an anomalous structure or an old organized membrane, for it was quite firm, deep pink, and not unlike the surrounding mucosa; Moreover, no other evidence of pseudomembrane was found. The larynx was impervious on probing.

Smears taken from the mucosa showed diplococci in a pure state. A small quantity of frothy mucus was blown up through the tube from the bronchi. The child was placed in bed breathing perfectly and with good color and pulse.

About one hour after operation the temperature was 103°; pulse, 130; respiration, 30. Stimulants were given freely. Next

morning at 3 o'clock the heart began to fail, and this continued until the following afternoon, when the child died, apparently from profound toxæmia. Just before death the temperature was 107° (per rectum); pulse, 150, and respiration, 50. At this time my incubator cultures developed sufficiently to show the absence of bacilli. The clinical phenomena were so unusual and suspicious that my bacteriologic findings were accepted, but not without some hesitation.

Case III.—A male babe, aged five years; had measles at the age of two years, but was otherwise well. The tonsils were chronically enlarged, and each winter he would have sore throat and "croup." On January 28th the child had one of its familiar attacks of sore throat, and three days later the voice was hoarse and the cough "croupy." During the night he had several choking spells. Next morning Dr. Seward was called, and he found the tonsils filling the throat, but no membrane. The symptoms at the time of his visit had subsided. In the afternoon drowsiness occurred, and all night the child struggled for air. Next morning Dr. Rind was called into consultation, and at this time the condition was so grave that he hastened for his instruments and assistants. I was called to make a throat examination. The patient was already on the table with the trachea opened. I took my culture smears through the wound and from the mucus blown out from the tube. Microscopically, the smears showed only diplococci, which were numerous. The mucosa appeared congested and the larynx was swollen shut, but no membrane was found. I was told that the child was blue and comatose before operation, and no anæsthetic was required. Antitoxin (5000 units) were given at the time of the operation. The breathing and color improved after the tube was in the trachea, but the pulse remained weak, and the child died about two hours after operation. At my request Dr. Vance procured a section of the larynx, the findings of which I shall report farther on in this paper.

Cases I. and II. lived in the same block; Case III. lived eight squares from the other two, and no evidence could be secured, making it probable that a contagion was carried from one to the other or from outside sources. It may also be stated that the three cases occurred in families in comfortable circumstances, and the hygienic environment was good.

The bacteriologic investigation of these cases involved about four months of research, a complete report of which would be impractical in this paper. I shall merely give a synopsis of this work.

Unfortunately, in Case I. the cultures were destroyed after a few days' growth. However, the essential characteristics of the organism, both microscopically and culturally, together with the extensive suppuration induced, leads me to believe that it was similar

to that found in Cases II. and III. In the last two instances the cultures were carefully grown in both incubator and room temperature. The findings in Case II. were as follows:

On moist streak agar pinpoint colonies were visible after twelve hours' growth in the incubator at 37° C. The mature colonies consisted of a slightly elevated slimy mass, with smooth wavy border, and varying in color from milky white to canary yellow. The color characteristic of the colony was often lost in transplanting. Blood serum tubes showed almost the same appearances.

In bouillon, rapid clouding with subsequent deposits of granular pigment was produced. Stab cultures in gelatin showed finger-shaped liquefaction with pigmented deposit in the pendent part. Gelatin plates contained pin-point grayish colonies which soon enlarged, giving rise to saucer-shaped depressions and final liquefaction of the medium. In litmus milk slow coagulation and acid formation occurred; the casein was subsequently liquefied. The cultural tests in Case III. were almost identical, excepting the pigment variation was less marked. Besides this a few of the original cultures were contaminated, owing probably to the fact that the field of operation could not be properly prepared, and dispatch was certainly paramount in this instance.

Microscopic examination of these cases proved the organism to be a coccus occurring single, more often in pairs, and frequently in clusters. The individual organism varied in size, which was especially noted in those composing the short chains found in the liquid media. The cocci stained both by simple aniline dyes and also by Gram's method. Variation in the intensity of staining was observed in many instances.

From the above observations I was assured that the organism was the staphylococcus. The irregular behavior of the pigment formation led me to omit any conclusion as to the prevailing type of staphylococcus involved.

Coincident with the cultural work the pathogenesis was determined by inoculating white mice. In Case I., as stated before, the cultures were destroyed. In Case II. the staphylococcus grown on blood serum for three days in the incubator (37° C.) was transferred to bouillon, and after twelve hours' growth was injected subcutaneously near the root of the tail in two mice. One received 5 drops and died within sixteen hours; the other received 10 drops and died eleven hours after inoculation.

Post-mortem examination of the mice showed slight changes, consisting mainly of congestion and moderate œdema of the tissues. Smears and cultures taken subcutaneously, intraperitoneally, and from the blood showed cocci in large numbers. Microscopic sections of the organs showed small numbers of the same organism. The peritoneal smears revealed marked leukocytosis, and many phagocytes loaded with cocci were witnessed with much interest.

The pathogenesis having been in a measure ascertained, I next attempted to determine the degree of virulence and probable means of accidental infection. Healthy mice placed in the infected cages remained well. Contamination of the food and drink with fresh cultures proved negative. After five weeks of incubator growth the organism in culture was again inoculated subcutaneously into healthy mice, using fresh bouillon cultures, but these failed to kill even in large doses. Abscesses, however, formed at the point of inoculation. Cultures attenuated by three months' growth in the incubator were next injected into the peritoneal cavity of white mice. They recovered from the inoculation of 5 drops of fresh bouillon culture, but 15 drops killed within twenty-four hours, and on post-mortem examination overwhelming numbers of staphylococci were demonstrated by smears, cultures, and sectioning of the organs.

Cultures from Case III. were similarly tested, and practically the same results were obtained. Larger doses for intraperitoneal injection were necessary to kill, which was either due to lesser virulence of the organism or more rapid attenuation by artificial growth.

The section of trachea removed from Case III. was sectioned and stained. Microscopically it showed small cell infiltration of the mucosa, submucosa, and muscularis. The mucosa had a few superficial erosions upon which were deposited masses of cocci. There was no evidence of fibrin or pseudomembrane. Staphylococci in small numbers were also found in the interstitial stroma of the submucosa and striped muscle bundles.

To briefly summarize the essential points, we have here three cases of preliminary sore throat in children, followed by severe obstructive symptoms in the larynx, and requiring tracheotomy. In none of the cases was there evidence of a pseudomembrane. The clinical symptoms pointed to a local infectious process with elaboration of toxins. In two of the cases the diagnosis of diphtheria was entertained, and antitoxin was given, but with negative results. Bacteriological examination revealed the presence of practically pure cultures of staphylococci in the trachea and larynx. The organism in recent artificial cultures proved to be unusually pathogenic to white mice. Subsequent inoculation of the same strain of bacteria proved much less virulent. Pathogenesis was displayed only by direct inoculation into the lymph or blood circulation.

From an analysis of this investigation we may safely draw the following conclusions:

1. The winter epidemics of tonsillitis and sore throat in children at times give rise to laryngeal complications.

2. This condition is always serious owing to the ease with which the juvenile throat may be obstructed.

3. Individual predisposition to laryngeal complication is quite probable.

4. The staphylococcus, a common denizen of the throat, may, under favorable conditions, give rise to grave symptoms, as exemplified in the above cases.

5. The rapidity of onset and severity of symptoms may at times suggest diphtheria.

6. A reliable bacteriologic examination of the throat is a prerequisite.

7. Antitoxin, although to be used in doubtful cases, will be of no service in cases in which the Klebs-Loeffler organism is not the causative factor.

8. The above may be taken as examples of cases at times diagnosed as diphtheria in which no microscopic examination is made. Moreover, the failures of antitoxin are often credited to such cases.

9. Finally, I would emphasize the importance of a careful analysis of each case, basing the diagnosis on both clinical and bacteriologic evidence.

A STUDY OF THE GROUP ACTINOMYCES.

WITH THE REPORT OF A PATHOGENIC SPECIES FOR MAN.

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Historical Review. Before describing the organism which was isolated from an abscess of the lung, I shall review some of the important points concerning the group actinomyces and its increasing importance in pathology.

In 1875 F. Cohn[1] described an organism which Foerster had found in the human lacrymal canal. This he described as a filamentous growth which showed true branching forms. Despite this description the organism and others resembling it were confused with cladothrix by a number of different authors. Even such men as Baumgarten[2] and Nocard[3] placed actinomyces and streptothrix du farcin du bœuf in the genus cladothrix. The demonstration of actinomyces by Nocard as the cause of a disease in animals soon caused investigators to study it more closely, and it was soon separated from cladothrix, since the false branching of this organism sufficed to distinguish it from a streptothrix with true dichotomous branching.

The streptothrix* since this time has been found in a large number of pathological and saprophytic conditions.

* The name streptothrix is used in an historical sense, but the name actinomyces is later given to the entire group.

Almquist[4] isolated one species from a case of meningitis, and found another variety in water, which gave a white growth. Gasperini[5] obtained streptothrix Foersteri from the air, and found a second species which was negative when inoculated into guinea-pigs and rabbits. This was chromogenic, forming a brown color.

The observations of Eppinger[6] are of special interest.

He observed a streptothrix in a case of meningitis and cervical abscess, which caused pseudotubercles when injected into the tissues of guinea-pigs and rabbits. The branching threads stained by Gram's method, and formed coccus-like spores. Gruber[7] also found one of these organisms which produced abscesses in guinea-pigs, and Doria[8] by exposing gelatin plates to the air cultivated thirty-five colonies of streptothrix alba of Gasperini, and seven colonies of streptothrix nigra. The four other chromogenic species were whitish-yellow, pink, orange, and violet. These species all seemed similar under the microscope, and formed spores. Sauvageau[9] also found two specimens of a streptothrix in gelatin plates exposed to the air.

Bollinger and Harz[10] first called the fungi found in actinomycosis by the name of actinomyces. Following this observation a large number of articles appeared on this subject. Boström[11] has studied and carefully described one form of streptothrix actinomycotica which is aërobic, and pathogenic for man and cattle, and not pathogenic for laboratory animals, such as guinea-pigs and rabbits. Wolf and Israel[12] soon described another species which differed from the former in growing best under anaërobic conditions, and in being pathogenic for small laboratory animals. They obtained it from two cases in human beings. Levy[13] found an anaërobic species in five cases of human actinomycosis, and Asthoff[21] isolated this species from a case of primary actinomycosis of the lung.

Streptothrix has been observed quite recently in a number of diseased conditions in animals and human beings.

Silberschmidt[14] found an organism in the lungs of a goat with a disease resembling tuberculosis. He called it streptothrix capræ. This species consisted of filaments staining by Gram's method, which grew on all the culture materials and produced abscesses or pseudotubercles in guinea-pigs and rabbits.

Aoyama and Miyamoto[15] described a form of streptothrix which they cultivated from the pus from a lung affected with caseous pneumonia and purulent pleuritis. The organism was present during life in the sputum. It proved as resistant to acids as the tubercle bacillus, but grew readily as a streptothrix on the various media, and produced pseudotubercles and fibrinohemorrhagic exudations in animals.

Two cases of necrotic bronchopneumonia have been recently reported by Norris and Larkin[16] as caused by a streptothrix. Both patients suffered from clinical conditions resembling lobar pneu-

monia, and at the autopsies the lungs showed complete consolidation, and one case also exhibited a fibrinous pleuritis. The lungs in both cases, upon histological examination, showed a necrotic or purulent bronchitis and purulent exudation in the alveoli with small diffuse abscesses. A few threads of the streptothrix were found in the air cells, but the necrotic bronchi contained many colonies of the streptothrix. The lung also contained many streptococci. These organisms were stained by Weigert's method.

Some difficulty was experienced in separating the streptococci from the streptothrix, but by cultivating the material from infected rabbits on sterile normal kidneys, and then transferring the colonies to broth, a pure culture was at last obtained.

This then grew on the usual culture materials, although it had first refused to do so. The injection of the streptococcus and the streptothrix together into rabbits produced suppurative and necrotic pneumonia and bronchitis, but when pure cultures of the streptothrix were injected into the tissues death did not often occur. These injections, however, caused abscesses, and pseudotubercles, and the organism can be considered as pathogenic.

Fullerton[17] found a pathogenic streptothrix in the case of a woman, aged forty-six years, who had suffered from a cough for twelve years. On admission to the hospital the patient had bloody expectoration and pulmonary rales, and an abscess in the left axilla and over the clavicle. The streptothrix was found in the sputum, and a pure culture showing mycelium and spores was obtained from the pus. It grew on glycerin-agar and broth, and was not pathogenic for rabbits. Scheele and Petruschky[18] also report a case of pulmonary infection due to this organism. The woman suffered from fever, thoracic pain, and pulmonary symptoms. Small tumors filled with pus appeared at different points under the skin. The streptothrix was found in the sputum and pus during life, and an ante-mortem diagnosis of streptothrix infection was made. At the autopsy the streptothrix was found in the solidified lung, and the metastatic abscesses. It grew on gelatin, and in bouillon.

In the chronic inflammatory process usually affecting the tissues of the foot called mycetoma, or Madura foot, a form of streptothrix has been isolated from one variety of cases. In the pus from the ochroid, or pale variety of the disease, granules have been obtained which grow on potato as a typical streptothrix. Vincent[23] and Boyce and Adams[19] have all probably cultivated a form of streptothrix from such cases, which belongs to a different species of the genus streptothrix from that of actinomyces bovis.

Sabrazès and Rivière[22] isolated a form of actinomyces from a case of abscess of the brain, lungs, and kidney. This organism stained by Gram's method, showed irregularity in staining, and true dichotomous branching. Its mixture with other bacteria

prevented its further study. Berestneff, in a Russian publication quoted by Hektoen, also reported a specimen of actinomyces asteroides which he isolated from an abscess of the brain.

It will be noted that thus far I have used the names which have been applied in a rather confusing way to the various species of this group. Hektoen[24] and later MacCallum[20] have pointed out that priority is alone valid in determining nomenclature, and after weeding out the various other names for this genus they correctly conclude that actinomyces must be used for all the species of this group. These organisms in the future will, therefore, be called actinomyces.

MacCallum also isolated a specimen of actinomyces asteroides from a case of general subacute purulent peritonitis in a child aged three years. This condition followed a gastrostomy for the relief of an œsophageal stricture. As this organism will be minutely described in the section on classification, no further comment will be made at this time.

Description of Case and Organism. The organism which I shall describe was obtained in pure culture from an abscess of the left lung in a case of marasmus in the service of Dr. John Ruhräh at the Garrett Hospital.

Clinical History. The child was a white male, aged twenty-eight days. The temperature showed no elevation, and the child died at last from wasting and exhaustion. Cyanosis was present, the spleen was palpable, and a few rales were detected in the lungs.

Record of Autopsy. The body weighed four pounds, and the cervical glands were enlarged. The subcutaneous and subperitoneal fat was light yellow and of a granular appearance. The thymus gland only weighed 2.1 grams, and measured 3.5 by 2 cm., being 6 mm. in thickness. This organ, therefore, showed the atrophy characteristic of marasmus.

The lower portion of the lower lobe of the left lung at the middle part of its diaphragmatic surface showed a small projecting area, which, on section, proved to be a pus cavity about the size of a pea. All of the other viscera were normal in appearance.

A culture from the abscess on blood serum gave a pure growth of the actinomyces to be described farther on.

Histopathology. *Lung Abscess.* The lung tissue surrounding the abscess is deeply congested, and the air cells are filled with an exudate consisting of red blood corpuscles and endothelial cells. The abscess itself simply consists of a collection of polymorphonuclear leukocytes, containing many branching threads staining by Weigert's method.

Lung. Left lung. The smaller bronchi are filled with an exudate consisting of polymorphonuclear leukocytes, red blood corpuscles, and cells with round nuclei surrounded by eosin-staining protoplasm. The lung tissue surrounding these bronchi has under-

gone great thickening, and is richly infiltrated with young connective-tissue cells with round, oval, or elongated nuclei. Many of the interalveolar septa are greatly thickened, and some of the air cells and infundibula adjacent to the inflamed bronchi are filled with pus cells. There is also marked congestion of the interalveolar capillaries. On staining sections by Weigert's method a firm network of branching threads is to be seen in the abscess. No coccus-like bodies or clubbed ends are present, and the growth consists entirely of threads.

Thymus Gland. Fibrous capsule somewhat thickened. The interlobular tissue is markedly thickened, cutting up the lobules into irregular masses. Some of these irregular lobules contain as many as fifty degenerated Hassall's bodies. These bodies are dilated, and they usually contain a central body composed of concentrically arranged hyaline material. Between this and the lumen there is usually a peripheral rim of polymorphonuclear leukocytes, although sometimes this rim is simply a clear space. This rim is surrounded by a single layer of flat cells resembling endothelium. There also seems to be an increase of reticular tissue and reticular endothelium within the lobules, and the lymphocytes are not as numerous as those in the normal gland. Sections were made from all of the other viscera, but no abnormal changes were found. Cultures from the viscera remained sterile. The macroscopic and microscopic changes, therefore, simply indicated a case of marasmus in which the terminal infection was caused by a species of actinomyces.

Description of the Organism. The serum tube, which was inoculated from the pus from the lung, did not show any growth for six days, and at the end of this time a number of fine, white, pinpoint dots appeared on the surface of the medium.

Morphology. In fresh specimens the colonies consist of branching threads about twice the transverse diameter of a typhoid bacillus. In the meshes of these threads and at the distal ends there are a number of round bodies free in the fluid.

When the colonies are teased out or gently crushed they can be mounted on a slide and stained by Gram's method. The threads are long and often show side branches. The staining is interrupted or irregular, areas of dark-blue protoplasm alternating with unstained areas of protoplasm. The spores are often grouped around the distal end of a thread, and are about twice the size of an ordinary micrococcus. There are also smaller round spores free in the field, often arranged in chains resembling streptococci.

Spores. When a colony is stained by the Ziehl-Gabbett method the numerous ovoid spores retain the red dye. Some of these spores almost resemble bacilli, although they are not as long and thin as the tubercle bacillus. Most of the hyphæ or threads of the colonies stain blue, showing no resistance to acids. A few, however, stain bright red, and these sometimes seem to cut off their ends by trans-

verse fission and form spores. These are the special hyphæ mentioned by Poncet and Berard in their book on *Actinomycosis*, which form the spores, while the ordinary mycelium does not form any spores. On staining with carbol-fuchsin the irregular, almost striped staining is well seen, but Loeffler's and Neisser's stains show no metachromatic bodies. This result differs from that obtained by MacCallum, who obtained many bluish-black metachromatic granules. He did not obtain any spores, but our results with the Ziehl-Gabbett stain certainly indicate the formation of spores. The threads in hanging drops are not motile.

Cultural Characteristics. 1. *Blood Serum.* The colonies form small, elevated, round, adherent dots of a golden-yellow color. The medium is not liquefied.

2. *Slant-agar.* The colonies are simply small white adherent dots which later coalesce into a yellow membrane.

3. *Sugar-agar.* The organism grows as a number of fine, elevated, brownish-yellow dots along the track of the needle.

4. *Potato.* The colonies appear as fine dots which later form a yellow spreading membrane. The growth is very adherent.

5. *Milk.* This medium becomes covered in one week with a thick yellow membrane, with elevations and depressions resembling a relief map. Litmus milk is rendered alkaline.

6. *Gelatin.* Not liquefied. Colonies are fine, white, adherent dots.

7. *Dunham's Solution.* A slight growth takes place in about five days, but no indol is formed even after two weeks.

8. *Nitrate Solution.* After two weeks' growth in the nitrate solution a few colonies are present, and a slight nitrite reaction takes place.

Fermentation Tube. The organism does not cause gas formation in glucose, lactose, and saccharose bouillon, and does not grow in the closed branch of the fermentation tube.

In glucose bouillon in a flask the growth is very luxuriant, and in one week a white membrane forms on the surface of the bouillon. This later becomes wrinkled, and at the end of a month the surface growth has formed a number of round, knob-like elevations, varying in size from that of a pinpoint to a diameter of 3 mm. Some of these knobs are white, some are a dull golden-yellow, and a few show a combination of both of these colors. The colonies seem to need but little nourishment, as they even develop on the sides of the glass which has been moistened by the bouillon.

The development in glucose bouillon in the fermentation tube or flask might be considered as characteristic.

Animal Experiments. A suspension of 2 c.c. of the organism from serum was injected into the abdominal cavity of a guinea-pig, and the animal died in four days. The slight exudate consisted of small lymphocytes, large lymphocytes, polymorphonuclear leukocytes, red blood corpuscles, and endothelial cells. The liver con-

tained a few dots resembling tubercles. Cultures from the liver and peritoneal exudate gave a pure culture of actinomyces.

A rabbit was also given 3 c.c. of a bouillon culture of one week's growth. The injection was made in the peritoneal cavity. The animal died in one week, and only a few yellow nodules containing actinomycetes were found scattered over the peritoneum. One white rat injected subcutaneously in the abdominal wall with 3 c.c. died in ten days. There was a small caseous area at the seat of injection, and the organism was isolated from this area, but the viscera were sterile.

Another guinea-pig received 2 c.c. in the abdominal cavity, and the animal died in twelve days. The report on the autopsy is as follows:

Guinea-pig; 3 c.c. of bouillon injected in abdominal cavity on February 25th. Died on March 9th.

Body emaciated. Inguinal glands enlarged. The abdominal cavity was free from any exudate, and quite dry. In various places to be mentioned below, there were solitary, gray, firm masses about the size of a tubercle, which always projected from the peritoneal surface. These pseudotubercles were found on the upper surface of the liver, on the parietal peritoneum, in the shrunken great omentum, on the surface of the bladder, the gall-bladder, broad ligament of liver, posterior abdominal surface of lower sternum, and the diaphragm. Only from one to three pseudotubercles were found in each of these situations.

The thoracic organs and the other viscera seemed normal.

Cultures were taken from the abdominal cavity and the liver, and actinomyces was recovered.

The last guinea-pig received an injection of 2 c.c. directly into the pleural cavity, and the animal lived seven days. The result follows:

Thoracic Cavity. The chest wall is deformed; the sternum, instead of being in the median line, is curved somewhat in the shape of an S, and has been thrust into the right mammary line. The anteroposterior line between the midsternum and the dorsal vertebræ is deflected to the right at an angle of 45 degrees.

The left pleural cavity contains some fibrinous adhesions binding the chest wall to the lung. The right pleural cavity in its posterior portion contains 10 c.c. of a thick bloody fluid. The entire dorsal curve of the vertebræ is deflected to the left, having lost most of its anteroposterior curve. The entire parietal and diaphragmatic pleura on both sides, especially in the intercostal spaces, contains numerous gray, pinpoint areas resembling tubercles.

Lungs. Both lungs are compressed, and their surfaces are covered in places with thick patches of yellow membrane. This fibrinous inflammation has also invaded the mediastinum as thick conglomerate pseudotubercles, and these grayish dots can also be made out on the parietal layers.

Lung Tissue. The lung on cut section is congested and contains many grayish, pinpoint pseudotubercles; the right lung presents a similar appearance.

Abdominal Viscera. The abdominal viscera are normal, with the exception of the liver; this contains a few yellow areas which look simply like distended vessels.

Microscopic Examination. One of the pseudotubercles from the mediastinum on being teased out consists principally of cells with large, round nuclei surrounded by granular protoplasm often containing fat-drops. There are also small lymphoid cells, and few kite-shaped or spindle cells. Here and there can be made out typical branching threads stained by Gram's method.

Gall-bladder. Gall-bladder contains many red blood corpuscles.

The cultures from the heart, kidney, and liver and lung tissue are sterile on blood serum and agar. The cultures from the pericardial cavity and both pleural cavities on blood serum and agar contain numerous typical colonies of actinomyces. The colonies on serum are of a golden-yellow color. These colonies, examined under the microscope, are typical examples of actinomyces, staining by Gram's method. It will be seen that this organism when injected into animals caused local nodules, either on serous surfaces or in viscera, which had a tendency to undergo necrosis.

Description of the Microscopic Changes Produced in Human Beings and Experimental Animals. In the cases reported by Eppinger, MacCallum, and myself the lesions in human beings simply consisted in a purulent exudation respectively in the brain and meningeal cavity, in the peritoneal cavity, and in the air cells of the lung. Aoyama and Miyamoto found fibrinopurulent pleurisy and an abscess of the right lung.

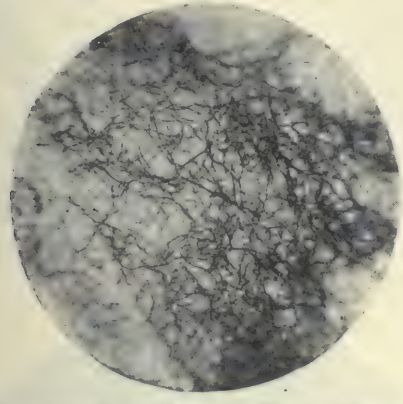
When the organism was injected subcutaneously in animals an abscess usually resulted, but when introduced into the general circulation or into any of the serous cavities a large number of small granulomata or so-called pseudotubercles were produced. These lesions thus differ from those described in human beings.

MacCallum has made a very careful study of the histogenesis of these lesions by studying the early changes in animals (in two rabbits) killed four and six hours after inoculation. The capillaries of the lungs were crowded with leukocytes. This was the first response to the presence of actinomyces asteroides. The lung of an animal killed twenty-four hours after inoculation already contained small nodules consisting of widely distended bloodvessels surrounded by alveoli, and their lumina were richly infiltrated with leukocytes. These nodules later undergo extensive necrosis, which process is the later result of the presence of the organism. These nodules never coalesce into larger distinct abscesses or cavities.

I was not able to confirm the early lesions described above, since I only examined animals that died at a much later period; but in

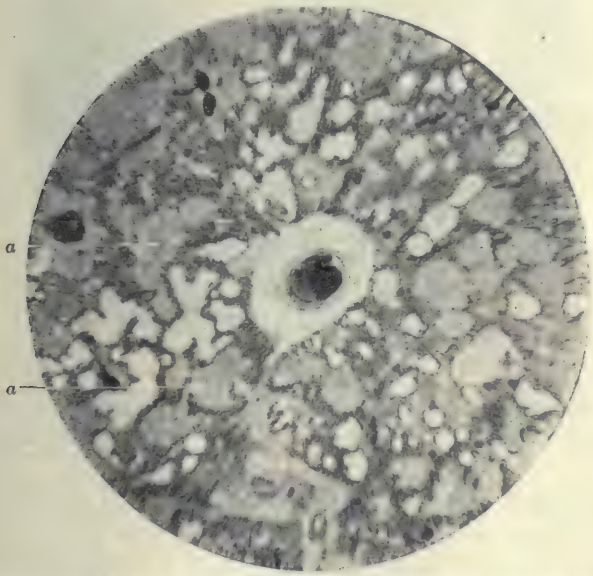
such animals numerous necrotic pseudotubercles were found in the lungs, liver, kidneys, heart muscle, and on the surface of the

FIG. 1.



This shows the twisted branching threads when stained from a culture of actinomyces asteroides by Gram's method.

FIG. 2.



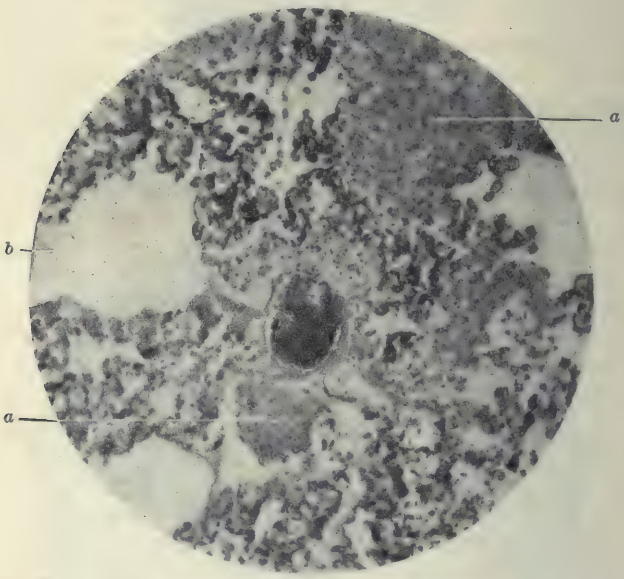
This is a picture of the lung of an injected guinea-pig when seen under the low power. In the centre is an artery, and below is a bronchus and several bloodvessels. The dark areas throughout the section are the pseudotubercles produced by the injection of the organism into the pleural cavity, the figure showing a necrotic nodule to the left of the artery, and another to the left of the bronchus (see "*a*").

various serous membranes. MacCallum did not find the typical production of lymphoid and epithelioid cells which precede necrosis

of the true tubercle, due to B. tuberculosis, but he found that the connective-tissue cells proliferate later and form a capsule of granulation tissue, which often contained giant cells. Our own experimental lesions often showed a similar proliferation of connective-tissue cells, in which small lymphocytes were often present. The photomicrographs show the various proliferating cells and the necrotic pseudotubercles in the lungs and heart.

Actinomyces asteroides thus produces a primary exudation of leukocytes, and, of course, organisms from the capillaries. In rabbits and guinea-pigs this is followed by necrosis and encapsulation of the injured tissue by a proliferation of the fixed tissue cells.

FIG. 3.



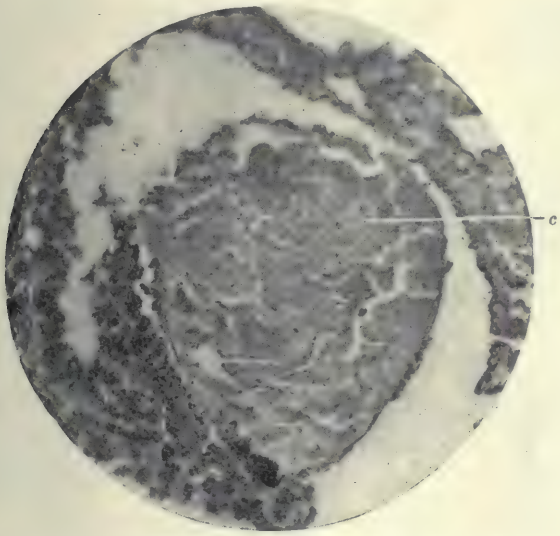
This shows several tubercles at *a*, and *b* indicates the proliferation of the fixed tissue cells around a vein in the centre of the picture. This is the final reaction to the organism.

Actinomyces Vesicæ. Through the kindness of Prof. Hugh H. Young, of Johns Hopkins University, I am also able to report an organism which he isolated by aspiration of the bladder in the case of a man, aged sixty years, at the Johns Hopkins Hospital.

The patient was suffering from chronic nephritis and uræmia, with retention of urine. About 1500 c.c. of urine were aspirated from the bladder, and much pus was found in this fluid. In addition a bacillus which could not be identified as any pathogenic organism was isolated, and an organism with long threads and true dichotomous branching was isolated in pure culture. This organ-

ism was called actinomyces vesicæ, and, as its cultural characteristics are completely described in the accompanying table, these will not be repeated at this time. Its main characteristic is the brilliant orange color that it produces in cultures, but it can be distinguished from the actinomyces asteroides by the fact that it liquefies gelatin, casein, and blood serum. It did not prove pathogenic when injected into guinea-pigs, either subcutaneously or in the pleural cavity, and it cannot be claimed that it caused the cystitis noted above. It is probable that it did, however, since a saprophytic bacillus was the only other organism found in the purulent urine, and it is embraced in this study with the expectation that it may be noted in other pathogenic processes.

Fig. 4.



This figure shows a section made through a papillary muscle of the left ventricle. The red blood corpuscles can be seen free in the cavity and surrounding the muscle, and the central portion of the papillary muscle contains a necrotic pseudotubercle produced by injection. The normal muscular structure and the necrosis and fragmentation of the pseudotubercle can be well made out.

Classification of the Various Species of Actinomycetes. On reviewing the literature concerning the various species of pathogenic actinomycetes it became apparent that several of the species described by different authors could be grouped as one species on account of their similarity. This classification has already been made by Silberschmidt, but the accompanying table includes species not described by him, as well as the pathological changes in men and animals. A few of the organisms have not been described completely enough for classification, but those which have been thoroughly described can be grouped as seven distinct species.

Name of organism and observers.	Morphology.	Motile.	Spores.	Gram's stain.	Metachromatic bodies.	Appearance on agar.	Appearance on blood serum.	Appearance on potato.	Gelatin plate.	Growth in bouillon.
Actinomyces bovis. Bollinger, Israel, Boström, and others.	Ray fungus consisting of a radiating mass of mycelium containing many spores in centre, showing evidence of true branching forms; at the periphery the threads terminate in clubbed ends.	0	+	+	0	Small opaque colonies which later show a white downy appearance, which coalesce into an adherent, wrinkled, lichen-like membrane.	Same as agar; the growth is slower and is of a yellowish color with a white shaggy deposit.	Same as agar; the blood serum liquefied.	Arborescent colonies which slowly liquefy gelatin.	Opaque glo ules like grape seed which coa esce into a loose flaky sediment; surface me brane form
Actinomyces asteroides. Eppinger, McCallum, Sabrezes et Riviere(?), Aoyama, Stokes, Berestneff.	Mycelium with branching threads ending in spores of an elongated appearance, and also showing clubbed ends.	0	+ Staining by the Ziehl-Gabbett spore stain.	+	+ Neisser's stain.	Small shaggy colonies which coalesce into a thick adherent membrane with elevations and depressions and of an orange color.	Same as agar; serum not liquefied.	A profuse white or yellow growth with a fine white feathery growth from upper surface.	Small, radiating colonies near surface with depressed centre and shaggy margins.	Beginning minute, whi shaggy colo ies like pu balls, they form a dens elevated an depressed y low surfac membran on surface
Actinomyces Israeli. Wolf and Israel, Norris and Larkin, Levy, Aschoff.	Short branching mycelium, with bulbous or clubb'd ends and coccus-like spores.	0	?	+	+	White pinhead sized colonies of a conical shape, not often coalescing.	Scanty white growth; very adherent.	Not observed.	Pinhead, later spreading colonies of whitish opaque colors.	Small disco fluffy gran ules, often adherent t sides of tub
Actinomyces Nocardi (du Farcin du Bœuf). Nocard.	Long thin hyphæ twisted in masses, showing many branching forms like cabbage sprouts or burs.	0	+ Resist ordinary stains	0	Not mentioned.	Small, white irregularly round, opaque colonies which form an adherent, thick, wrinkled membrane-like lichen.	Same as agar, but moister in appearance.	Grows rapidly as small, scaly plaques, which form a projecting dry pale yellow growth.	Not observed.	Irregular white mass which fall t bottom of tubes, but gray lentic lar membr forms on th surface; n change of neutral or a kaline sug bouillon.
Actinomyces Maduræ. Vincent.	Many twisted filaments showing true branching forms, and staining irregularly. The mycelium shows a ray-like growth at the periphery, but no true club forms; some of the hyphæ show nodular enlargement along their course.	0	+	+	+	Small, projecting, round whitish-yellow colonies, which slowly take on a rose color; they show an umbilication in the centre and become confluent and adherent to the medium.	Do not develop on blood serum.	On the fifth day at 37° C. numerous small white colonies appear with a mammillated aspect; the growth remains white.	Small colonies with a filamentous periphery; no liquefication of medium.	Small, floa ing, inde pendent zoogleal, white ball which slow sink to bot tom of tub
Actinomyces capræ. Silberschmidt	Twisted branching filaments which break off at the end into forms resembling bacilli or cocci; a few of the shorter forms show clubbed ends.	0	+	+	Stains irregularly.	In two or three days dry, verrucose, shrivelled, brownish-white colonies appear which form an adherent, brown, irreg'lar membrane in from eight to fifteen days.	Colonies in four to eight days which form a dry brown coat.	Round, dry, crater-like colonies which later form a pinkish brown coat on the surface.	White colonies with a dense brown centre, and a clear periphery showing many projecting filaments.	Colonies d velop on su face as co cave, fine, d pale disk which late form a su face mem brane; flui clear, but deposit for in the bott of tube.
Actinomyces vesicæ. Young.	Mycelium twisted, showing irregularity in size and staining; a few ovoid gonidia growth from side of hyphæ which show true branching forms.	0	0	+	0	Brilliant orange-colored groups like seed often piled on one another, resembling a cone; very adherent to agar.	Same as agar; serum slowly liquefied.	Brilliant orange-colored adherent growth.	In three days many round orange colonies with finely granular centre and many projecting threads under low power.	Large, pal yellow ba with oran centre an fine fuzz surface.

'ermenta-ion tube; glucose.	Lique-faction, gelatin, casein, serum.	Gelatin stab.	Nitrate reduced.	Indol produc-tion.	H_2S.	Litmus milk reaction.	Chromo-genesis.	Pathogenesis.
o fermen-ation of glucose; aërobic.	Liquefies serum, casein, and gelatin.	Arbores-cent growth which liquefies gelatin.	Positive marked reaction.	Well-marked reaction after standing for 24 hours.	+	Dirty yellow mem-brane on the sur-face; re-action alkaline.	Slight yellow color.	Pathogenic for bovines and human beings; producing a subacute, diffuse, purulent inflammation, with the for-mation of granulation tissue
ferment. c growth closed nch; thick pical yel-w-white, vated and epressed embrane surface of n branch; ërobic.	0	No lique-faction; growth arbores-cent.	Very slight reaction.	Very slight reaction: Sabrezes et Riviere 0	+ Sabrezes et Riviere 0	Thick yellow elevated and de-pressed mem-brane on surface; reaction alkaline.	Orange yellow color; Sabrezes et Riviere light yel-low to chocolate brown.	Subcutaneous injections pro-duce purulent abscesses, and injections into circulation or serous cavities produce ne-crotic nodules in the various viscera of rabbits and guinea-pigs; the organism produces purulent inflammation in human beings. Sabrezes et Riviere 0.
ferment, rowth in th arms; cultative aërobic; ows only t 37° C.	Casein not liquefied.	No growth at 20° C.	0	No growth in Dun-ham's solution.	.....	Acidu-lated and coagu-lated.	0	Intraperitoneal injections produced necrotic nodules in the peritoneal cavity and viscera containing the acti-nomyces; often these nod-ules contained purulent centres surrounded by a zone of granulation tissue. Same as A. bovis for human beings.
fermen-ion, and ly grows the open ranch; aërobic.	0	No lique-faction.	Not ob-served.	Not ob-served.	0	No coagu-lation or acidula-tion; remains neutral.	0	In bovines the organism pro-duces purulent inflammat'n of lymphatic glands; intra-venous or intraperitoneal injection into guinea-pigs causes the formation in vis-cera and peritoneal cavity of many small nodules which contain pus and the organ-isms; subcutaneous injec-tion produces pus formation
fermen-on growth n open ranch; obic; no wth in a cuum; O_2 or H.	Gelatin and blood serum negative; casein dissolved	Abund-ant white growth along track of needle; no lique-faction.	Not ob-served.	Not ob-served.	Not ob-served.	Coagu-lated and later the casein is dissolved	Light yellow to red on agar.	Not pathogenic for laboratory animals; in human beings the organism produces a pseudotubercle of the ex-tremities consisting of a cen-tral zone of mycelium in-filtrated by polymorphonu-clear leukocytes surrounded by a second zone of regener-ating tissue containing fibro-blasts, newly formed capil-laries, and masses of red blood-corpuscles.
fermen-ation.	Gelatin, blood serum, and casein not liquefied.	Not de-scribed.	Not ob-served.	Not ob-served.	Not ob-served.	Not co-agulated; rose col-ored mem-brane on surface.	Varies from white to rose color and brown.	Subcutaneous injections caused purulent abscess in guinea-pigs and rabbits, and intravenous injections pro-duced generalized tubercles which contained giant cells and underwent caseation. Isolated from the lung of a goat containing many pseudotubercles.
as forma-, aërobic faculta-e anaër-obic.	Liquefies gelatin, casein, and blood serum.	Fine light orange line.	Marked reaction.	0	0	Reaction acid.	+ Bright orange color.	Guinea-pigs injected sub-cutaneously and into pleural cavity were observed for one month and then killed; no lesions were found.

Actinomyces bovis can be distinguished from four of the other species by its failure to infect small laboratory animals, and from actinomyces Maduræ by the failure of the latter to liquefy blood serum or gelatin. The anaërobic species, actinomyces Israeli, can be distinguished from all other species by its preference for an anaërobic medium, and especially from actinomyces bovis by its production of necrotic pseudotubercles in guinea-pigs and rabbits. Actinomyces asteroides can be easily separated from actinomyces bovis by the failure of the former to liquefy blood serum and gelatin, by its bright golden-yellow appearance, and by the production of pseudotubercles in laboratory animals. It also differs from actinomyces Nocardi in its yellow color, and in producing an alkaline reaction in milk, while the latter remains neutral and white. Actinomyces Maduræ differs from actinomyces capræ by the former's failure to infect small laboratory animals, by the rose color of the former, and the brown color of old cultures of the latter, and by the liquefaction of casein by actinomyces Maduræ. Practically all of the species described (see table) can be placed in these seven groups.

Chemical Products of Actinomyces Asteroides. MacCallum attempted to produce a soluble toxin from cultures in bouillon about three weeks old. These were filtered through a Pasteur filter, and the filtrate, in doses of from 6 to 10 c.c., was injected into rabbits without any ill effects. The writer grew this organism for one month in neutral bouillon and then filtered it through the Pasteur filter, and preserved this fluid by 0.5 per cent. carbolic acid.

Two guinea-pigs, weighing about 300 grams, were injected with 0.5 and 0.1 c.c. of the fluid, and they died in ten days. The lungs were congested, and microscopic examination showed intense congestion of the lungs, liver, and kidneys. Two more guinea-pigs were injected with 0.1 c.c., and one died in twenty-four hours. The seat of injection, the liver, and the lungs were all congested. The other pig remained well.

These experiments indicate that the organism forms a soluble poison for guinea-pigs.

Conclusions. The various forms of pathogenic actinomycetes can be classified at present as seven species, which produce suppuration or necrotic pseudotubercles in man and various animals.

The generic name for this group should be actinomyces, since the other names have been previously used for other organisms.

Cases resembling tuberculosis but failing to show tubercle bacilli should be carefully examined for the presence of actinomyces.

In concluding, I desire to thank Mr. John Johns and Dr. John S. Fulton for the photomicrographs, and Dr. Caleb Rohrer for assistance in the pathological study.

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ASSOCIATED MOVEMENTS OF THE HEAD AND EYES IN INFANTS.[1]

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AND

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THE various forms of movements of the head and eyes in infants—the so-called rotary and nodding spasms of the head and vertical, horizontal, and rotary nystagmus—are observed quite commonly. The obscurity of their origin makes them especially interesting. For this reason Dr. Posey and I have decided to present these three cases, which happen to be attending our services in the Howard Hospital at the present time.

CASE I.—Carl C., aged three years, first came to the children's clinic in the Howard Hospital on October 13, 1903. The history recorded at that time was as follows: His birth was normal, and his first dentition complete. His parents are living and well, save that his mother is thought to be nervous. He has no brothers nor sisters, and his mother has had no miscarriages. His previous health has been excellent. He has had none of the infectious diseases of

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childhood, and has never had any convulsions. For some time he has complained of abdominal pain. For many months he has lived chiefly on two cups of weak tea with each meal, milk, bread, and butter. He never eats meat. He eats freely of ice cream, but of other sweets rarely.

The condition which brought him to the dispensary was a cough of two days' standing which was accompanied by fever at night. The cough had a tendency to be paroxysmal, and the paroxysms were sometimes severe; it was tight, and there was no expectoration. He had some epigastric pain, and his bowels had been loose for several days. He had several stools each day, which were yellowish and watery, but contained neither blood nor mucus.

The physical examination showed a well-nourished child. His tongue was heavily coated, and its papillæ red and prominent. His frontal and parietal eminences were prominent; there was moderate thickening of the epiphyses at the wrists and ankles. There was some costochondral thickening and some retraction of the base of the chest, more marked on the right side; there was moderate dorsolumbar lordosis and decided outward bowing of the tibiæ. His abdomen was prominent; its walls flaccid, and there was marked separation of the bellies of the recti. His spleen was not palpable, but his liver was felt a finger's breadth above the transverse umbilical line, about three inches to the right of the umbilicus. There were a few scattered moist rales over each lung. He had a fairly loud, low-pitched, blowing systolic murmur, best heard in the aortic area and transmitted especially well to the top of the sternum and into the subclavians, less well into the carotids. A murmur of similar character was heard over the body of the heart, at the apex, in the axillary region, at the angle of the scapula, and in the interscapular space. At the apex the murmur was the same in character as that heard at the base, but in this area it seemed to occur later in systole; the second sound was heard distinctly over the upper chest.

On November 15th he had a mild follicular tonsillitis. On March 10, 1904, he was brought to Dr. Posey's clinic in the Howard Hospital on account of movements of the head and eyes and reduction in vision. These manifestations were first noted early in December. They had increased persistently up to this date. The head movements were lateral and not constant, the head apparently being drawn to the right and the chin slightly elevated, as if by action of the left sternocleidomastoid muscle. The eye movements were also from side to side and constant, the excursions being fairly extensive.

He was unable to recognize objects at a distance of four or five feet, but when brought within this range they could be defined. Any attempt at fixation caused a decided increase in the excursions of both the head and eye movements, especially the latter. Covering the eyes produced a temporary cessation of the movements of

the head, and they ceased during sleep. There was some restriction to the movements to the right in both eyes.

An examination of the eye-ground by Dr. Posey showed some engorgement of the veins, but no other abnormality. The only other nervous phenomenon noted was a slight uncertainty in his gait, and a mild ataxia, which had never been sufficiently marked to attract the father's attention. His reflexes were normal.

Further questioning showed that in December he had had a slight discharge from one ear, which cleared up quickly. About the same time he developed a cough, which has persisted. He has occasional severe paroxysms, which the father says sound like whooping-cough. Usually it is loose, but without expectoration. He vomits during or immediately after almost every meal. He does not seem to be nauseated, and frequently eats immediately after vomiting without being sickened. He never vomits at other hours of the day. His bowels continue loose—four or five stools each day—which are watery and yellowish in color. He voids urine frequently and in large quantity. Two examinations of the urine showed nothing abnormal, except a lowered specific gravity —1014 and 1012. Dr. F. R. Packard kindly examined the ears, throat, and nose, and reported nothing abnormal.

Case II.—R. E., aged seven months, came to the Howard Hospital Dispensary on March 24, 1904. His birth was normal; his parents, three brothers, and one sister are living and well. One brother died aged two years of "baby consumption." He has had no convulsions, no manifestations of syphilis, and no previous illness. He has been fed exclusively on the breast about every third hour.

He was brought to the dispensary on account of a coryza of one week's duration; the discharge was free, and consisted of thin mucus without blood. His respirations were snoring in character —a condition which had existed since birth. There were no evidences of sore throat, but he had a cough in the beginning of the attack which was croupy in character. He has had no gastro-intestinal symptoms.

The mother first noticed shaking movements of his head and eyes between the third and fourth months, and for some time he has had profuse head sweating. He is thought to have gained steadily in weight. He has always been a mouth-breather, and constantly chokes while nursing, as if there was some obstruction to nasal breathing. He seemed quite bright, and had no fever.

The physical examination showed a fairly well-nourished infant. There was no evidence of nasal membrane. His uvula was swollen and red. The fauces and tonsils were red, but without exudate. His tongue was moderately coated. His head was narrow in the bitemporal diameter, and the posterior fontanelle was still open. The coronal, sagittal, and lambdoidal sutures were wide open, and there was marked craniotabes along the borders of the squamo-

parietal and mastoparietal sutures, especially evident on the right side. He had a bald spot over the occiput. His neck was short, and the sternum elevated. His clavicles were on a direct plain with the body, and probably elevated slightly at the sternoclavicular junctions. His chest was markedly violin-shaped, his costochondral junctions were much enlarged, suggesting on palpation a backward dislocation of the cartilages. The portion of the chest wall between the costochondral junctions was pushed forward. The epiphyses were thickened at the wrist and knees, and there was slight dorsolumbar kyphosis. His abdomen was prominent, the bellies of the recti muscles were separated, and there was some pouting of the umbilicus. He had a frequently recurring spasm of the muscles of the back of the neck, with retraction of the head. Similar muscle spasms were not noted in other groups. His inguinal, axillary, epitrochlear, suboccipital, postcervical, and a few of his deep cervical glands were enlarged. He had marked lateral and tilting to-and-fro movements of the head, the head rotating to both sides as if by alternate contractions of the sternocleidomastoid muscles.

Dr. Posey's report upon the eye condition showed "lateral nystagmic movements with very short excursion and of similar extent in each eye. There were no apparent ocular palsies. On near fixation the movements were much increased, and this was associated with increased movements of the head. The examination of the eye-ground showed nothing abnormal."

On April 8th it was noted that the infant had emaciated decidedly, although his general condition seemed better; his head and eye movements were less.

Case III.—Lilian B., colored, aged eleven months, applied for treatment at the Howard Hospital Children's Dispensary on August 13, 1902. Her birth was normal.

Family History. Both parents are living and well, but a paternal aunt and uncle died of phthisis. The child had had no previous disease, but had always been "poorly." She had been breast-fed for the first four weeks of life, since which time she had been fed on cows' milk, bread, crackers, cakes, candy, ice-cream, chocolate, and potatoes. She was brought to the dispensary for a cough, which she had had for three or four months. She was sometimes feverish, and had occasional night-sweats. Her cough was most severe at night. Her bowels moved six or seven times a day, the stools being yellowish in color, very loose, malodorous, and containing curds, but no mucus.

Physical Examination. The child was emaciated. The anterior fontanelle was very large, the sutures open, and the posterior fontanelle still open. The chest was markedly violin-shaped, and there was beading of the ribs. There was some epiphyseal thickening, the abdomen was very prominent, the umbilicus pouted, and there was separation of the bellies of the recti muscles. The

heart's action was regular and rapid, and the sounds clear. The breathing was labored, and the respiratory movements were increased in frequency. There were no areas of dulness. There was a wheezing sound on inspiration. The chest was full of sibilant and sonorous rales, by which the respiratory murmur was masked. There were no areas of bronchial breathing. The spleen was palpable just below the costal margin, and the liver one-half inch below. The cervical, anterior and posterior, the axillary and inguinal glands were moderately enlarged. The body temperature was normal.

The child made three return visits from this time up to the middle of October, 1902, and then disappeared until February 24, 1903. She was brought back on account of the return of the cough of the previous winter. She had recently had an otitis media on the left side. At the time she returned she was having a great deal of nasal discharge. Her appetite was poor, her cough loose, and attended by considerable expectoration. She slept well, but sweated a great deal about the head at night. It was noted at this time that she had a marked lateral nystagmus, which was said to have existed since the third month. It was much more marked in the right eye, and was at first thought to have been unilateral. There was no history of head movements at any time, nor of muscular twitchings in any other part of the body. At the age of sixteen months she had only her upper and lower middle incisor teeth. The anterior fontanelle was as large as a dollar, and the sutures were separated some distance from the fontanelle. There was marked bowing of the bones of the forearm, eversion of the legs, without much bowing of the bones, except a slight anterior bowing of the tibiæ. The spleen was palpable a finger's breadth below the costal margin. The child was very weak, and required considerable assistance in order to maintain an erect posture. There were a few rales over the chest. The physical examination otherwise showed no changes.

Following this the child was absent from the dispensary for about eight months, when she returned with an aphthous stomatitis. Five months later she returned suffering from prolapse of the rectum. She was having three or four stools daily, accompanied by straining. They contained mucus, and there had been a slight amount of blood in some stools. This developed sometime after the prolapse of the rectum. Prior to this time the bowels had been normal. The abdomen was very much distended. There was no vomiting. The spleen was not palpable, the liver was two inches below the costal margin. There was no evidence of prolapse of the rectum found on examination.

The child returned twice following this, the last time on March 30th, on which occasion it was announced that there was no longer any prolapse of the bowel. A careful physical examination showed nothing to account for the prolapse. She had never vomited. She had no abdominal signs of any significance.

She is twenty-six months old at the present date. Her eye and stomach teeth are just erupting. All of her teeth are in poor condition and immaturely developed. One lower incisor has been lost by being caught in the thread of her skirt, indicating that the attachment of the teeth is insecure. The examination of the eye condition by Dr. Posey shows that when at rest the nystagmus is limited to the right eye; the movements are lateral, and the excursions very short. On fixation, or when the eyes are removed from the primary positions, slight nystagmic movements appear in the left eye also. There does not seem to be any limitation in the movements of the eyeball in any direction. Once or twice during examination, when the attention was suddenly attracted, there was a marked vertical vibrating spasm of the upper lids. Excitement increased the nystagmic movements, but the movements were not increased when the head was held fixed.

The question of the *etiology* of these phenomena remains unsettled. Numerous theories have been advanced, and the more recent writers have been in some accord in relation to this point. That the condition is dependent upon some functional disturbance of that part of the nervous system controlling the movements of the head and eyes is generally conceded. While it is not our purpose to treat this subject exhaustively it may be well to briefly review some of the more important theories that have been suggested.

Predisposing Causes. Age is an essential predisposing factor, the vast majority of cases occurring between the ages of two and twelve months, although Gee has reported a case occurring as early as the sixth week, and Henoch one as late as the third year. The cases are pretty evenly divided among the sexes with a slight majority in favor of females.

Heredity is supposed to play some part, in that a number of cases have occurred in families of bad nervous history, including epilepsy.

Rickets is probably the most common predisposing factor. In his early series of cases Hadden found this condition present in but two of eleven. On the basis of this finding he attached but little importance to it. In his second series of nine cases he found it present seven times, after which he modified his views decidedly. Other authorities differ as to its etiological relationship, the majority considering it an extremely common factor. The remarkable frequency of rickets, especially of its milder forms, would lead us to believe that its association has probably been closer than statistics would indicate. We are of the opinion that the milder manifestations of rickets, the head sweating, delayed dentition, and moderate beading of the ribs, but more especially the muscle and nervous phenomena, are of very frequent occurrence, and that, because we are prone to depend upon the skeletal deformities for our diagnosis, the manifestations in the nervous system—irritability, night terrors, etc.—and the muscle phenomena—pot-belly, gastric and intestinal

distention, constipation, etc.—are apt to pass unrecognized. In the dozen or more cases seen by one of us rickets of some degree was manifest in each.

Exciting Causes. Dentition was thought by Henoch to be the most common, because the conditions occurred during the period of first dentition, and because in some of his cases its beginning was coincident with the eruption of some of the first set of teeth. Most authorities admit that it may act as a contributing cause, but that it does not occupy the important position attributed to it by Henoch is manifest from the fact that many recorded cases have occurred at an age which would eliminate the teeth as a disturbing element.

Gastrointestinal irritation has preceded its occurrence in many cases, and it is generally conceded to be an important factor. It may act either reflexly or through the medium of toxic products absorbed from the intestinal tract.

Traumatism was recorded in a number of Hadden's cases, and in those of Peterson and Hirsch. Peterson thinks it probable that concussion is the determining factor in most cases—"a concussion setting up in the centres of the spinal accessory, and at times in those of the oculomotor nerves, an arrhythmic discharge."

Our knowledge of the pathology of these movements, for obvious reasons, is mainly speculative. Hughlings Jackson considered the condition a variety of "spinal system chorea, a symptomatic condition akin to canine chorea," while Gunn believed it was in some way associated with epilepsy, basing his view upon the quite common occurrence of temporary loss of consciousness in these cases, and the presence of epilepsy and other nervous conditions in the families in which they occur. Henoch previously suggested the same view, and Hadden, whose cases were the basis of Gunn's suggestions, gave this opinion some consideration.

Henoch, in describing his cases, suggested that the concomitant existence of these head-and-eye movements "seem to indicate that the root nuclei of the spinal accessory and of the upper spinal nerves supplying the affected muscles of the throat and neck stand in a very close relation to those of the ocular nerves (occulo-motorius)," a relationship which has since been definitely determined. Hadden believed that "the seizures pointed to instability of motor centres above the nuclei in the spinal cord and fourth ventricle, therefore attributing the disorder to a functional or other disturbance of the cerebral cortex. The child has acquired certain voluntary or purposive movements of the head and eyeballs, but these have not as yet become thoroughly organized and fixed in the psychomotor areas of the brain, hence a dissolution takes place because of the inability of the strained cortical centres to stand the work to which they have been too early subjected." This opinion, quoted by Mills, is one which he believes "throws the best light on an obscure subject."

Aldrich, in his very able discussion of this condition, voices the same view as to the nature of the condition. As we have stated, while we are by no means certain that the nature of these conditions is definitely determined, we incline to accept Hadden's explanation.

These three cases differ to some extent in the character of the head and eye movements. In Case III. the head movements are lacking entirely, the nystagmus is mainly in the right eye, and, according to the mother's statements, has existed since the third month. A point of special interest in this case is the occurrence of the vertical movements of the upper eyelid on an attempt at sudden fixation, a feature which has been noted but once before.

In Case II. the movements began at a very early period—between the third and fourth months—and involved both the head and eyes. They were equal on both sides. There was present in this case an intermittent spasmodic contraction of the muscles of the back of the neck.

In Case I. the movements began at an unusually late period—after the time that such movements have ordinarily disappeared. The head movements in this case are caused mainly by spasmodic contraction of the left sternocleidomastoid muscle, and the eye movements are the same on the two sides. In addition, there is some evident defect of vision and a slight ataxia, a somewhat similar condition having been noted in one of Hadden's cases. This is the only case in which it was possible for us to demonstrate any limitation in the excursions of the extraocular muscles.

Strabismus was not noted in any of the cases. There have been no antecedent nervous conditions from which the head and eye movements might have resulted, and none of them have had any of the acute diseases of childhood except Case I. The pupils were of normal size and reacted normally in all three cases, nor were there any changes in the fundi other than the dilatation of the retinal veins noted in Case I. The eyes in all three cases were moderately hypermetropic.

While the head-and-eye movements are manifested in a somewhat different way in each of these cases, and while we have been unable to elicit a history of head movements in one of them, we are, nevertheless, of the opinion that they are all dependent upon some form of irritation of the cortical areas.

The extreme rachitic manifestations present in all the cases marks this condition as the underlying or predisposing factor. The exciting cause in Cases II. and III. are difficult to determine. They both developed before the age of dentition, there is no history of injury, and they did not suffer from acute diseases which might have acted reflexly or by the development of some toxic irritant, or by suddenly producing increased instability of the motor centres, from the resulting exhaustion. The early age at which they became

manifest and the striking rachitic condition which was present lead us to believe that the toxic products resulting from the disturbed metabolism due to the rickets were the irritating factors in these cases. In Case I., however, the conditions are different. The rachitic manifestations in the child were much later, but very marked, quite sufficient to interfere with the nutrition of the nervous system.

The movements began in this case about two weeks after an attack of bronchitis, which was associated with diarrhœa, the latter condition persisting up to the present time. Furthermore, this child has been partaking most intemperately of tea for many months, regularly drinking two cups with each meal. The bronchitis, diarrhœa, and tea drinking, therefore, acting in a markedly rachitic child, we consider quite sufficient to have produced the phenomena noted.

A point of interest in these cases is the relationship which exists between the movements of the eyes and head. In an article which was read by one of us before the fifty-third annual meeting of the American Medical Association, entitled "Associated Movements of the Head and Eyes," the close association which exists physiologically between the movements of the head and eyes was dwelt upon, and it was shown how the head by its movements augments the range of the field of vision and supplements the action of the extraocular muscles in the delicate task of maintaining proper visual axes. Attention was also called to the fact that in order that the head may properly perform this twofold task it is provided with numerous and intricately acting muscles, and it is only when one considers that there is scarcely a position assumed by either the eyes or head in which the action of both parts does not enter that one realizes how intimate the relationship between the extraocular and cervical muscles is.

To facilitate the study, all associated movements which exist between the head and the eyes were divided into four groups. The first group referred to movements which are physiologic and will require no further mention here. The second group included abnormal simultaneous but independent movements, such as occur, for example, in disseminated sclerosis, where the movements which are abnormal and often simultaneous and have the same pathogenic origin are not related in the sense of being dependent upon one another. The third group dealt with compensatory movements. To this class were relegated cases which assumed a vicarious position of the head to compensate for some imperfect action of one or more of the extraocular muscles, such, for example, as occur after paralysis of one or more eye muscles. The fourth group referred to related but not compensatory movements, and included movements of the head and eyes which are abnormal and bear a distinct relationship to one another without being dependent upon

one another. Cases of head-nodding in children, such as have been presented to the Society to-night, were included under this latter group, although it was realized that there are a number of reasons why they should have been placed under the third group and the movements of the head considered to be secondary to those of the eyes. Thus, it is a well-established clinical fact that movements of the head, apparently similar to those observed in this class of cases, may originate in children whose eyes oscillate as a consequence of lowered vision, occasioned by a disease of the eyes, and it has been noted not infrequently that nystagmic adult patients hold their heads in a peculiar position while fixing for both distant and near objects, and often succeed in steadying the oscillation of the eyeballs in this manner. It has been remarked, too, in cases of the affection under discussion, by both Raudnitz and Caillé, that if the eyes are bandaged the motion of the head ceases. Raudnitz noted also, in common with other observers, that the head movements were much influenced by the deviation of the visual axes, that they ceased when the eyes were deviated in certain directions, and started up again as soon as they were rotated from this position. This writer thought that the disease was particularly apt to arise in the dark winter months and to affect those confined in darkened rooms, believing that the head-jerking was secondary to the nystagmus, the latter being occasioned by strain upon the eyes consequent upon the infant's constant attempt to look toward the windows. Notwithstanding these observations and the well-established fact of the possibility of movements of the head being inaugurated by those of the eyes, it is probable that such is not the case in head-jerking, the movements occurring in association by reason of a common cause affecting the centres controlling each simultaneously, but without being dependent upon one another.

While in most instances the data which have been gathered regarding the time of the occurrence of the nystagmus and of the head-jerking are obtained by questioning the parents, and are, therefore, not entirely reliable, still there is evidence to show that the nystagmus does not always precede the head-nodding, that the head-nodding may even be observed some weeks or months before the jerking in the eye muscles manifests itself, and that, finally, head-jerking may occur without the occurrence of nystagmus during the entire course of the disease.

Moreover, in order that the movements of the head should compensate and neutralize those of the eyes, they should be directly opposite to one another; such a condition, however, has been found in but one case, the motion of the head being either in the same direction as those of the eyes, or, what is more usual, without any connection with them whatsoever. Again, the movements of the eyeballs are usually twice as rapid as those of the head and have their own rhythm.

It has been suggested that the presence of a strabismus in some of these cases would indicate that the nystagmus, under such conditions, at least, was the primary factor, but while the strabismus may indicate a palsy of one of the eye muscles nystagmus does not follow palsy of the eye muscles under other conditions.

A STUDY OF A CASE OF SPLENOMYELOGENOUS LEUKÆMIA.

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(From the medical service of Dr. Wainwright.)

The subject of this study was previously under the care of Dr. J. Emmet O'Brien, of Scranton, and Dr. Thompson, of Carbondale, to both of whom we are indebted for notes of his former history.

The patient stated that about six years before admission to the hospital he had a severe attack of abdominal pain, with vomiting and diarrhœa. He said that this illness was similar to his subsequent ones. He was given arsenic at the time, and made a good recovery, and was apparently in good health until late in the year 1902, except for a time in 1901, when he was bothered by a pain in the splenic area.

About October, 1902, he began to suffer again with "bloating" and with alternate constipation and diarrhœa. Dr. O'Brien first saw him on December 11, 1902. He found the spleen much enlarged. A record of the blood count was not kept, but it is known that the leukocytes were much increased in number, and smears showed the picture of a leukæmia of the splenomyelogenous type. Fowler's solution in increasing doses was prescribed. On January 3d the patient returned much improved, and the splenic tumor was not palpable. On January 28th the spleen could again be felt, and the leukocytes were still numerous. His general condition, however, seemed to be improved. He was last seen by Dr. O'Brien on March 24, 1903.

From March, 1902, until his admission to the hospital he was seen a few times by Dr. Thompson, who was called chiefly for gastrointestinal trouble. One of these attacks yielded to small doses of calomel daily. At another time he was again given arsenic, with benefit.

On the whole, during this period his condition was fairly good, He seems to have been troubled only by the attacks of diarrhœa, and he kept very steadily at his active duties as inside foreman of a coal mine until March 31, 1904.

The patient was admitted to the Moses Taylor Hospital on April 14, 1904.

Family History. Father died of miners' asthma[1] at the age of sixty-six years. Mother well at sixty-eight. Grandparents died of old age. Has one sister, aged forty-six years, and one brother, aged forty years. Both have always been well. One brother died of violence at the age of twenty-six years. He has been married twenty-one years. Wife is well. He has seven living children, all of whom are well. Three other children died in infancy of convulsions, diphtheria, and enteritis, respectively.

Personal History. He is forty-one years old. Was born in Wales. Came to this country when two years old. At ten he started to work in a coal breaker. At eleven he began to work inside the mines as a driver boy. He was for many years a miner, and for the last fifteen years has been inside foreman. He has worked continuously inside the mines for thirty years.

He has used alcohol and tobacco only in moderation, and denies venereal infection. There is no history of malaria.

Present Illness. In addition to the notes above he stated that while he did not give up work until two weeks before admission he had been gradually growing weaker for the past seven months, His only complaints have been a feeling of tightness in the epigastrium, "swelling of the stomach, which made him short of breath," and frequent attacks of vomiting and diarrhœa. About a week ago he began to have severe occipital and frontal headaches. For four months his feet have been slightly swollen, and for several months he has had a dry cough.

Physical Examination. An emaciated man of small stature, looking ten to fifteen years older than his correct age. There is a marked general pallor of the skin and mucous membranes, with a slight yellow-lemon hue. There are no hemorrhagic areas visible. The throat looks normal except the tonsils, which are a little reddened and swollen. There is no stomatitis. The muscles are small and flabby, and there is very little adipose tissue. Pulse, 100; temperature, 99°; respirations, 24.

Thorax. This is rounded and thickened anteroposteriorly. Its lower portion is bulged forward, forming a well-marked Harrison's groove on both sides. Lungs normal. The heart is either enlarged or displaced upward. The dulness from the upper border extends to the second interspace; the right border to the right edge of the sternum. The apex beat is felt in the fourth space one inch to the left of the midclavicular line. The first sound at the apex is weak; the second aortic is slightly exaggerated.

* This is a term which is very loosely used in the coal regions and covers almost anything in the way of chronic bronchitis, emphysema, myocarditis, chronic nephritis, phthisis, or even the general failure of old age.

The arteries are prominent and tortuous and markedly thickened. The pulse is full and firm. Tension is not raised (132 mm. in radial by Riva-Rocci).

Abdomen. The left costal margin is bulged forward more than the right, and there is a visible tumor in the left hypochondrium. On palpation this tumor is evidently the spleen. The spleen is stony, hard, and smooth; the edges are sharp and well defined, but no notches can be felt. At this time the mass is not painful or tender. The upper border of splenic dulness is at the sixth space in the anterior axillary line. The right edge is felt one inch from the median line, and the lower margin is on a level with the antero-superior spines. The liver is also considerably enlarged. The dulness of the upper border begins at the fourth rib in the mid-axillary line. The lower border can be felt about one inch above the level of the umbilicus. It is not especially hard or sharp. There are no prominent veins over the abdomen.

The *eye-grounds* are somewhat pale, and the vessels look a little soft and flabby. There are no retinal hemorrhages.

The *urine* is pale, slightly turbid; specific gravity 1017; a small amount of albumin is present, and also a few granular casts. There is no sugar.

A blood examination the day after admission shows hæmoglobin, 58 per cent.; red cells, 2,500,000; white cells, 692,000.

DIFFERENTIAL COUNT OF 500 LEUKOCYTES.

Large and small mononuclears	8.0	per cent.
Transitional cells	2.0	"
Polynuclear eosinophiles	4.0	"
Polynuclear neutrophiles	37.5	"
Myelocytes, eosinophiles	3.5	"
Myelocytes, neutrophiles	45.0	"

In this count there were found several nucleated red cells, several mast cells, but no megaloblasts.

History after Admission. Second day: Severe attack of epistaxis. Ceased spontaneously. Slight diarrhœa. Sleeps badly.

Third day: Diarrhœa relieved by opium and bismuth.

Sixth day: Diarrhœa very troublesome again. Put on increasing doses of Fowler's solution.

Ninth day: Diarrhœa persists in spite of medication.

Thirteenth day: Hæmoglobin, 56 per cent.; red cells, 2,100,000; white cells, 620,000.

Fourteenth day: Pain in abdomen during urination. No hæmaturia. Has been voiding thirty-six to forty-six ounces daily. During next three days a marked diminution of urine. Returned to usual quantity under citrate of lithium.

Twenty-second day: Fowler's solution discontinued as patient begins to show physiological effects. Marked coryza. Hæmoglobin, 54 per cent.; red cells, 3,010,000; white cells, 208,000. The spleen is

considerably diminished in size. It is three inches below costal border, and seems softer. Liver also diminished in size.

Twenty-fourth day: Fowler's solution recommenced. Another attack of epistaxis.

Twenty-eighth day: Has had sore throat for several days. Throat congested, but no hemorrhagic areas. Now has severe pain in left ear, and slight deafness. No tenderness over mastoid. Arsenic again has to be stopped.

Thirty-first day: Still sleeps badly. Weight, 103 pounds. Spleen still smaller. Lower border only one inch below ribs. Liver also smaller. Apex beat of heart is now in fifth space. Drum membrane has ruptured, and there is a profuse bloody discharge from the left ear. Hæmoglobin, 60 per cent.; red cells, 2,971,000; white cells, 44,300.

Thirty-third day: Left ear drum punctured by Dr. Murray. This was followed for six days by such profuse bleeding that canal had to be tamponed. Puncture relieved pain, but deafness is steadily increasing. An organic iron preparation given.

Thirty-seventh day: Fowler's solution, gtt. xv, t. i. d., again begun.

Fortieth day: Has been constipated. Weight, 103½ pounds. Specific gravity of blood, 1041; hæmoglobin, 62 per cent.; red cells, 3,430,000; white cells, 22,000.

Forty-fifth day: Weight, 105¾ pounds. Spleen and liver still felt about one inch below ribs.

Fifty-second day: Weight, 109½ pounds. Fowler's solution increased 1 gtt. daily.

Fifty-ninth day: Hæmoglobin, 50 per cent.; red cells, 2,260,000; white cells, 54,000. Deafness increasing in both ears. Has been up about ward, but now returned to bed on account of weakness. Spleen a little larger. Is two inches below ribs, and liver three inches. Weight, 110 pounds.

Sixty-fourth day: Has been eating very little, and yesterday and to-day has vomited frequently. First elevation of temperature since admission. Highest is 102° at 8 P.M. Next day 102.4° in evening. Evening temperature continued like this until death.

Sixty-fifth day: General abdominal pain for first time. No tenderness.

Sixty-eighth day: Diarrhœa again troublesome. Fowler's reduced to gtt. xviii, t. i. d.

Seventieth day: *x*-ray over spleen for eight minutes; five ampères; distance, nine inches. Diarrhœa checked with opium.

Seventy-second day: *x*-ray over spleen for twelve minutes; six ampères; distance six inches.

Seventy-third day: Fowler's solution reduced to gtt. x, t. i. d. Strychnine, gr. $\frac{1}{40}$, every four hours. *x*-ray to spleen for nine minutes; five ampères; distance seven inches.

DIFFERENTIAL COUNT OF 500 LEUKOCYTES.

Large and small mononuclears	9.0	per cent.
Transitional cells	5.0	"
Polynuclear eosinophiles	0.5	"
Polynuclear neutrophiles	22 0	"
Myelocytes, eosinophiles	0 5	"
Myelocytes, neutrophiles	63.0	"

During this count one megaloblast, seven normoblasts, and a few poikilocytes were found. Myelocytes are not uniform in size, many being much smaller than at the first count. Many of their nuclei stain faintly and show signs of degeneration. A few mast-cells present.

Seventy-fourth day: Eyelids reddened and complains of photophobia. Deafness is now complete. Complains of severe pains over liver and spleen, and attributes this to the *x*-ray. Patient says he can "feel the *x*-ray working" during treatment. *x*-ray discontinued on account of patient's weakness, which is progressing rapidly.

Hæmoglobin, 32 per cent.; red cells, 1,920,000; white cells, 7000 (!). (Count verified).

Seventy-fifth day: Very restless; complains of severe abdominal pain. Respirations very labored. Dulness, harsh breathing, and moist rales over both lungs behind. Coma about noon, and death at 6.30 P.M.

Autopsy Fifteen Hours after Death. Rigor mortis slight; post-mortem lividity in dependent parts. Emaciation marked. Abdomen prominent.

Left Lung. Pleural cavity dry. A few slight adhesions at base. Deposits of coal-dust on parietal pleura. Lung weighs twenty-seven ounces. Crepitant all over except at base, where there is considerable hypostatic congestion. There is a marked general anthracosis. No tubercular scars.

Right Lung. Pleural cavity dry. There are a few slight adhesions at both apex and base. Anthracotic deposits on parietal pleura. Lung weighs thirty-one ounces. Pleura at apex is slightly contracted, but there are no definite signs of tuberculosis in the lung substance. Hypostatic congestion at base, but less marked than on left side. Same condition of anthracosis.

The *bronchial glands* and the glands around the lower part of the trachea are markedly anthracotic.

Heart. Pericardium is normal. Contains about one ounce of clear fluid. Heart weighs ten ounces. Muscle tissue pale. A small chicken-fat clot in left ventricle. Aortic and mitral valves are normal. No atheroma of arch of aorta. Papillary muscle pale. No zebra stripes. Ventricular wall of normal thickness. Chicken-fat clot in left ventricle. Pulmonic and tricuspid valves normal.

Spleen. Very dense adhesions to diaphragmatic peritoneum and to intestines. Weight, 52 ounces. Longest diameter, 21 cm. The

cut surface is very firm, dark-red connective tissue, trabeculæ stand out prominently; the Malpighian bodies are not distinct. There is an old infarct at the upper pole, two inches in diameter on the surface; it is evidently undergoing fatty changes. The splenic pulp surrounding this infarct is markedly hemorrhagic. There are also numerous hemorrhagic spots in other portions of the spleen. In the lower part of the organ there are two other smaller infarcts.

Liver. Weight, 77 ounces. Color pale and waxy-looking. There is slight retraction of the cut edges of the capsule. Moderate degree of chronic congestion.

The general *peritoneum* is normal. Foramen of Winslow patent. The gall-bladder, urinary bladder, and pancreas are normal. There are several anthracotic glands around the head of the pancreas. There are no anthracotic glands in the lesser omentum. The mesenteric and retroperitoneal glands are not enlarged.

Alimentary Canal. There is marked chronic congestion of the mucous coat of the stomach, with considerable post-mortem digestion. There is also a marked congestion of the upper half of the small intestine. Large intestine is normal. Appendix normal, directed down and in toward pelvis. No trace of Meckel's diverticulum. No intestinal parasites.

Kidneys. Both similar. Weight, 5 ounces each. Capsule strips easily. Cut surface is rather pale. Cortex of normal thickness, and markings fairly distinct.

Prostate of normal size.

The *bone-marrow* of the ribs is dark red and does not present other unusual features. The marrow of the humerus is deep red, firm, and stands out prominently from the broken ends.

Microscopic Examination. (Tissues fixed in formalin and alcohol.)

Liver. There is some slight increase in the connective tissue. The liver parenchyma cells are fairly normal. They do not show fatty degeneration. The frequently described deposits of white blood cells are numerous. They are most prominent around the central veins and seem to consist principally of mononuclear cells and myelocytes. The central veins are generally empty, but many of the smaller arterioles seem to be plugged with leukocytes. There are a few small areas of extravasated blood among the liver cells in which the leukocytes are numerous. The capillaries of the liver are not dilated.

Lungs. These show the usual changes from anthracosis which are common in those who have worked a long time in coal mines. There is a considerable deposit of coal-dust in the walls of the air vesicles, in the connective-tissue septa, under the pleura, and around the bronchi and bloodvessels. There is some thickening of the walls of the air vesicles, and there is an increase of connective tissue around the larger deposits of dust. There is but little

swelling and desquamation of epithelial cells, as is sometimes seen in those who have worked in the mines up to a few days of their death. There is no sign of a tubercular inflammation. The alveolar capillaries are not distended. At the bases of the lungs there is the ordinary picture of hypostatic congestion. In some places where there is an increase of connective tissue due to the anthracosis there are large deposits of leukocytes.

Heart Muscle. This shows quite a marked degree of fibrous myocarditis. The muscle cells are separated in many places by large patches of fine, poorly staining fibrillar connective tissue, with a few spindle-shaped nuclei. There are no deposits of white cells in the sections examined.

Pancreas. Normal.

Kidneys. These are but little changed. No special increase in the connective tissue. The glomeruli are normal. There is some swelling and cloudiness of the cells of the secreting tubules. No deposits of leukocytes are seen.

Alimentary Canal. Sections from the portions of the stomach saved show but little mucous membrane. The subserous and muscular coats are normal. Sections from the small intestine are normal.

Lymph Glands. The only glands preserved for cutting were those around the trachea. In these the deposit of coal-dust is so great that the fine structure is entirely obscured.

Spleen. (Stains by eosin and Delafield's hæmatoxylin, picro-acid fuchsin, carmine, borax, eosin, and methylene blue.) Sections from the infarct show no splenic tissue, but only dense fibrous connective tissue, with a few poorly formed bloodvessels. Surrounding the infarct in the splenic tissue there is a diffuse infiltration of old, much degenerated, blood. Throughout the splenic tissue proper the most marked change is an enormous increase in the normal connective tissue. This is represented both by an increase in size of the trabeculæ and by an increase in the intercellular reticulum. The Malpighian bodies are nowhere well formed and prominent. Throughout the splenic pulp there is a considerable infiltration of blood cells, which are in some places much degenerated; in others they are comparatively fresh. In the pulp the predominating cell is, of course, the small round lymphoid cell. In the blood cells extravasated in the splenic pulp there are a larger number of normoblasts and also more megaloblasts apparently than were seen in the smears during life. There are also many cells resembling the myelocytes, but considerably changed by the hardening process. A few of these latter show distinct mytotic figures. This was not noted in the blood during life. In a prolonged examination of the sections one polynuclear eosinophile leukocyte was seen. As usual in miners, there are many fine coal-dust particles scattered diffusely throughout the intercellular spaces of the spleen.

Bone-marrow. Smears from the ribs and humerus taken at the autopsy and stained by the blood methods show the same elements as the circulating blood, except that the normoblasts and megaloblasts are much more numerous. There are a few eosinophiles. Pieces of the ribs and humerus were decalcified in 5 per cent. nitric acid, hardened in alcohol, and stained by the same methods as the spleen. These sections show more marked changes from the normal than any other tissue examined. There are no fat or large "marrow" cells, and the whole appearance closely resembles that of well-formed granulation tissue. There is a fine connective-tissue reticulum, in the meshes of which there are cells which vary much in morphology and staining properties. Most of these cells are round and somewhat larger than a red cell. Their protoplasm is homogeneous, and takes the eosin faintly. They have a quite small, round, homogeneous nucleus. There is another, less frequent type of cell, which is larger, oval, granular, stains deeply with eosin, and has a large granular oval nucleus. There are a few very large cells resembling myelocytes, but it is difficult to trace much resemblance between the cells previously found in the circulating blood and those in the marrow sections after treatment by nitric acid and alcohol.

The Blood Picture. There is little to note in the red cells. They stain well; there is no polychromatophilia. Poikylocytes and normoblasts were noted, especially toward the last of the disease, and were not very numerous at any time. Megaloblasts were also present in small numbers. These were about three times the size of an ordinary red cell, and, while the nucleus was sometimes irregular, none showed definite mitosis.

The myelocytes which predominated were quite characteristic in type. As the total number of leukocytes diminished the morphology of these cells also changed. Many were much reduced in size, the nuclei stained faintly, and the granules became less prominent. The eosinophile myelocytes were also characteristic. These gradually fell in number from 3.5 per cent. to 0.5 per cent. of all leukocytes. And in the last slide examined none were found. The polynuclear eosinophile leukocytes, which at first showed a relative increase, also diminished, and finally disappeared as the disease progressed to its termination.

The accompanying chart graphically shows the course of the blood changes as determined by weekly counts.

Among the points of interest in this case are:

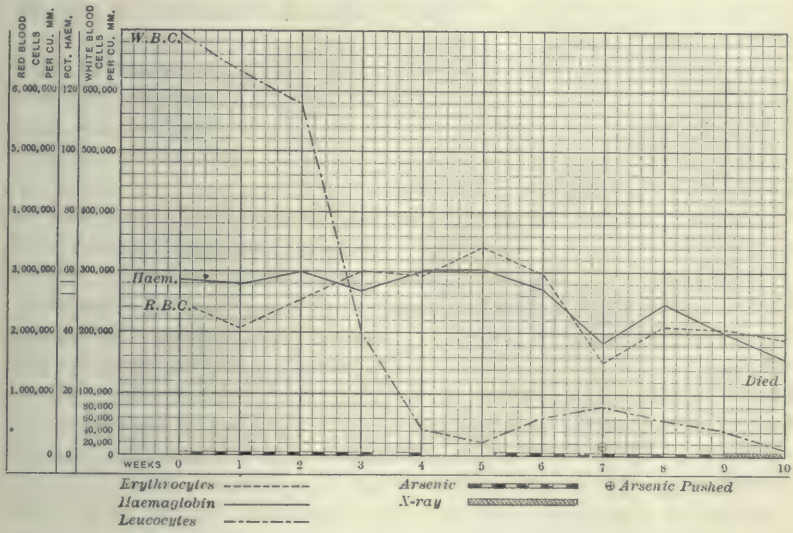
1. The fact that the man performed the active duties of an inside mine foreman for certainly two and probably six years after his disease began, and that he continued work up to ten weeks before the fatal termination.

2. The high leukocyte count of 692,000. We have not made an exhaustive search of the literature on this point, but among some

forty recent cases in easily available journals there was not given a higher count in chronic cases. An acute case of Hamman[1] and another quoted by him gave 958,000 and 790,000, respectively. While in exceptional cases the white may equal or exceed the red cells, our proportion of 1 : 3.6 is much above the average.

3. The disappearance of the previously increased eosinophiles. This fact, taken with Simon's case noted below, would tend to show that an increase in the number of eosinophiles is not so important a feature of this disease as has been considered.

4. An interesting symptom in this case was the deafness, which began in the fourth week of his stay in the hospital, and finally became complete. Deafness, while mentioned as a symptom in text-books—*e. g.*, Osler—is not spoken of in any case we have



reviewed, except that of Mott.[2] Mott attributed its presence in his case to hemorrhage into the middle ear. That this is the true cause is well demonstrated in our case, as a hemorrhage actually did occur and spontaneously perforated the membrane. Bleeding was profuse for several days.

5. The great prominence of intestinal symptoms throughout the disease, suggesting autointoxication from the intestinal tract as a possible cause.

The most interesting questions arising in the study of leukæmia are connected with its etiology and with the relation of the different forms to each other.

During the last few years the infectious theory of its origin seems to be rapidly gaining ground. The acute leukæmias certainly seem to be infectious in origin, and the frequency of pharyngeal and

tonsillar inflammation as a mode of onset cannot be ignored. The acute form of the disease, aside from its origin, frequently shows a decidedly septic type. Fussell, Jopson, and Taylor[3] noted this in thirty-one out of fifty-six acute cases which they collected.

Vehsemeyer placed leukæmias among autointoxications from the intestinal tract. As noted above, our own case suggests this, as diarrhœa was a prominent symptom throughout, especially at each exacerbation of the disease. During one of these, while under Dr. Thompson's care, he improved under small doses of calomel continued daily. Some of the exacerbations seem to have been relieved simply by a selected diet.

Simon's[4] case had recurring attacks of dysentery for twelve years before the apparent onset of the leukæmia. Diarrhœa was also a marked symptom in the previous history of Jewett's[5] case and of Miller's[6] case.

The much-quoted case of Obrastow, in which an attendant on a case of leukæmia also developed the disease in a few weeks, and one of Jewett's cases, in which a brother and sister seem to have had leukæmia, also point to an infectious disease. These cases in themselves are not, of course, conclusive.

Chmelar[7] fairly sums up the present status of the question when he says of leukæmia: "It has no specific cause, but arises under the influence of various acute and chronic infectious diseases, which alter and lead to excessive proliferation of the lymphoid elements." It does not seem that there is any connection between leukæmia and coal-mining, as this is the only case in a miner found in the last five years in the board of health records of Scranton, which has the largest coal-mining population in the United States.

The trend of opinion on the other point of the disease most under discussion—*i. e.*, the relation between the different clinical forms of leukæmia—seems to be toward the view that there is no specific difference between lymphatic and myelogenous leukæmia, but that they both are closely allied forms of fundamentally the same pathological condition. It would seem that the former sharp differentiation from the blood picture alone is little more than symptomatological. Indeed, if the hæmatologists are to make the classifications they will have to assume another form to include Simon's case of the myelogenous type without eosinophile cells. It would, perhaps, be as logical to consider tuberculous peritonitis with serous diffusion a specifically different morbid entity from the same disease with fibrin and adhesions.

The evidence as to fundamental unity of the two forms has now become a fairly logical chain, and is well summed up by Reed.[8] There seems little doubt now but that the acute and chronic forms are different only in the clinical course. While the acute type is generally the lymphatic, the myelogenous form does occur, as shown by the cases of Hirschfield and Cabot.

The first step in the evidence of the real identity of the two forms came in 1870 from Neuman. He showed that in each form the changes in the bone-marrow are marked. Reed's case, among others, seems, as she says, "to prove conclusively that we have here a lymphocytosis arising from proliferation of cells in the bone-marrow, and death occurring before any other organs showed involvement."

The establishment, too, of a mixed form of the disease further tends to show the close fundamental relation between the forms of leukæmia, and it seems that we will ultimately have to accept Reed's conclusion that "there are three forms of leukæmia, all due to myelogenous changes, and that they should be known as myelocytic, lymphoid, and mixed varieties, if we wish to make the blood picture the basis for clinical divisions."

The treatment of the disease is also an interesting feature. The value of arsenic, while real, is seldom more than temporary, though Simon and Campbell[9] report one case in which for a year the splenic tumor has been absent and the number of leukocytes normal. The authors believe that this is the only case on record showing this long-continued improvement. In our own case, as stated above, the disease was apparently held in check for probably six years by courses of arsenic.

The x-ray treatment is very promising, but its permanence cannot at this date be said to be proven. Heinke's[10] experimental work seems to show that the rays have a definite selective action, causing changes of a retrograde character in the spleen and lymphatic glands. From our present idea of the disease, however, this would apparently be attacking only a secondary result. Its curative action on the bone-marrow has yet to be demonstrated.

In our own case nothing can be inferred from the marked fall in leukocytes shortly after commencing the use of the rays, as the change may have been an ante-mortem one.

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ON TWO CASES OF WEIL'S DISEASE COMPLICATED BY THE TEMPORARY APPEARANCE OF SMALL TUMORS IN THE LIVER.

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Small palpable tumors of the liver are found in malignant neoplasms, and more rarely as a result of gummatous changes of this organ. The first end fatally, the latter may be cured by long-continued antisyphilitic treatment; without these measures the latter are also permanent.

A temporary occurrence of tumors in the liver, which disappear again in the course of a few days, has not been mentioned in literature as far as I know. I have, however, observed two such cases, and believe that it would be of interest to describe them here somewhat minutely and to add some remarks.

Case I (*December* 1, 1903). —August R., aged sixty-seven years, has been suffering for many years from his stomach and bowels. His appetite used to be fickle, and he was occasionally troubled with diarrhœa. During the last two or three years the patient was much better; he could eat better, felt stronger, and had a regular action of the bowels. The present trouble began three or four days ago. The patient felt weak, his appetite disappeared, the bowels were constipated, and severe headache was present.

Status Præsens. Pulse, 110; temperature, 101° in the mouth. In the thorax below and behind there are a few dry and moist rales. The hepatic dulness begins in the right mammillary line at the lower margin of the fifth rib, and extends one to two fingers' breadth below the costal margin. By means of palpation two protuberances of walnut size are distinguished in the right lobe of the liver; the liver and these tumors feel harder than normal. The left lobe of the liver is also swollen and sensitive, but does not exhibit any tumors. The spleen is enlarged.

The urine, of a specific gravity of 1023, shows the presence of albumin and casts.

Patient received 15 grains of calomel and was placed upon a strictly liquid diet.

December 2d. Temperature fluctuates between 103° and 104°. Urine contains some bile pigment and a great deal of albumin, no sugar; the diazo reaction is positive; Widal negative.

The patient complains of headache, cough, and weakness. The nervous system is perfectly free. The skin and scleræ are jaundiced, otherwise the condition is the same. Patient is given liquor ammon. anis., and heroin.

Since December 5th the temperature curve ran lower, and on the 8th returned to normal. The liver now shows no tumors, and is less swollen; the urine is free from bile and albumin. The cough disappeared and patient began to feel better and stronger. About fourteen days later the patient was perfectly well.

CASE II. (*April* 26, 1903).—Frederick S., aged about fifty years, was taken sick three days ago with vomiting and diarrhœa, loss of strength, insomnia, and fever. There was absolute anorexia and constant nausea, with frequent vomiting.

When I examined the patient I found a pulse of 100, temperature 102°. His face was flushed, tongue strongly coated; speech indistinct and stuttering; slight tremor in the hands. Color of skin and scleræ is slightly icteric. The abdomen is somewhat distended, the epigastric region markedly sensitive to pressure. The hepatic dulness begins in the right mammillary line at the upper margin of the sixth rib and extends two to three fingers' breadth below the costal margin. The consistency of the liver is harder than normal. On the convex surface of the right lobe there are three hard tumors of the size of a walnut, which can be easily palpated and are sensitive to pressure.

The splenic dulness is considerably enlarged, but the organ cannot be palpated. The urine is strongly concentrated, contains much sugar, albumin, and casts; diazo reaction is strong, and traces of bile are present. The patient complains of severe abdominal pains, vomiting, bad taste in the mouth, and insomnia, as well as of a harassing dry cough. He was given sodium bicarbonate and codein; liquid diet, veronal.

April 27th. Patient has slept, with interruptions; complains of a severe diarrhœa; says the stools smell very fetid. His condition is about the same as on April 26th. Widal reaction and malarial plasmodia are not found. He is ordered codein and tannigen.

30th. Fever is still present, but shows larger remissions. General condition is somewhat better. Objectively we still have the same symptoms of spleen and liver swelling; the urine contains albumin and sugar, but no bile. The diarrhœa has disappeared, vomiting and nausea no longer exist, and the patient can take nourishment better; he has a clear mind and speaks naturally.

May 2d. Temperature reaches only to 100.4°, pulse being 76; the nodes on the surface of the liver are less prominent and not so easily palpated; the liver is less swollen and less sensitive to pressure. Spleen is also smaller, the urine contains no sugar, shows no diazo reaction, but still traces of albumin.

5th. Temperature is normal; the liver projects only a finger's width over the margin of the ribs; the nodes cannot be palpated. The color of the skin is clearer, the splenic enlargement has disappeared, and the patient feels better in general, but is still quite weak. The urine is free from sugar and albumin. He began to

be up and about now daily and to take more food. In the course of five to six weeks the patient was completely well.

Epicritic Remarks. Both cases show a marked resemblance in their main features. In both the disease began, after a short prodromal stage, with fever, severe gastric disturbances, and general weakness. During the period of fever which lasted about a week, a marked enlargement of spleen was found as well as of the liver. Albumin was present in the urine, as well as a diazo reaction, and a trace of bile pigment in both, whereas sugar was found only in one case. Both had bronchitis. Cerebral symptoms, insomnia, severe headache, and disturbances of speech (some stuttering) were present in one case but not in the other. Widal's test was negative in both cases, and plasmodia were not found in the blood. After about a week's illness convalescence takes place. The fever and the albumin in the urine disappear; the gastric disturbances abate, and the swelling of the spleen and liver decreases, so that in the course of a few days these organs appear perfectly normal. There remains a condition of weakness which, however, disappears in the course of a few weeks, and the patients are then perfectly well. What is most remarkable in these cases is the fact that during the height of the disease small hard tumors appear on the hepatic surface which again entirely disappear with the abatement of the fever.

The clinical picture of these cases corresponds in the main to the symptom-complex described by Weil,[1] differing, however, from it by the transient formation of nodes of walnut size on the surface of the liver. With regard to the origin of the latter we may assume that this process in the liver is analogous to that of the acute nephritis existing in these cases (as evidenced by the albumin and casts in the urine). In other words, we probably have to deal here with an acute hepatitis with particularly prominent, severely affected, circumscribed foci. These nodes may be caused by an accumulation of exudative products, which again disappear with the subsidence of the inflammation.

Hepatitis resulting in a cure is often encountered. Budd[2] published some observations on this point which were later confirmed by Frerichs.[3] In Budd's book I find the following: "There are probably various morbid states of the secreting substance of the liver in which, as in erysipelas of the face and in the affections of the joints in rheumatic fever, the fluids poured out during the inflammatory process become again absorbed, leaving no permanent traces or only such traces as cannot be well distinguished. In such cases the nature of the morbid process can be judged of by

[1] A. Weil. Ueber eine eigenthümliche mit Miltztumor, Icterus und Nephritis einhergehende acute Infectionskrankheit., Deutsches Arch. f. klin. Med., 1886, Bd. xxxix. p. 209.

[2] George Budd. Diseases of the Liver, 1857, p. 167.

[3] Frerichs. Krankheiten der Leber, vol. i.

the symptoms only, unless the patient happened to die during the acute state of the malady and while its effects are still present."

Further on he says: "I have met with several instances in which enlargement of the liver has come on, and more than one in which jaundice has come on, soon after the disappearance of the rash and scarlatina; but I have never had an opportunity of inspecting the liver in a case of this kind. It is most probable that the disease of the liver is analogous to the disease of the kidney which so often occurs in scarlatina after the disappearance of the rash, and that the enlargement of the liver results from rapid development and shedding of the secreting cells caused by the elimination of some noxious matter through the gland."

The occurrence of palpable tumors (of about the size of a walnut) of the liver, which again disappear with the inflammation, is, however, not mentioned either by Budd or by Frerichs. Nevertheless, I believe that we have to deal here with a similar process.

The fact that distinctly palpable tumors of the liver may occur, existing only a few days in order to disappear again, must be of interest in a high degree, the more so as they cannot be differentiated by palpation from malignant or gummatous tumors. If, therefore, we meet such tumors in a patient suffering from fever, it is best to wait with the diagnosis of cancer or gumma of the liver until further observation permits a definite diagnosis.

VOLUMETRIC DETERMINATION OF THE PURIN BODIES (URIC ACID AND THE PURIN BASES) IN URINE.[1]

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AND

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The object of this paper is to describe an exact and clinical method of determining the uric acid and the purin bases in the urine. A great many methods have been devised for this purpose, the simpler ones being, as a rule, inaccurate, and the more exact ones of a complex nature requiring a great deal of time and a degree of technical skill not possessed by the average practitioner of medicine.

All the more exact methods are founded upon the property of uric acid and the purin bases of forming definite compounds with silver in an ammoniacal solution of the latter in the presence of

[1] Read before the New York County Medical Society, March 28, 1904.

neutral salts of the alkaline and alkaline earth group, preferably chloride of magnesium, chloride of lithium, or chloride of ammonium. Under the above conditions uric acid combines with silver in the proportion of one molecule of the former and one atom of the latter; the purin bases in the proportion of two molecules of xanthin to one of silver. The compound of silver urate formed under the above conditions is, as we shall show later, insoluble in both weak and strong ammonia up to 1: 200,000 parts. The compounds of silver and purin bases are soluble in strong ammonia, insoluble in weak ammonia.

In the standard method of Ludwig-Salkowski the procedure is as follows: A known quantity of urine is precipitated by a solution of silver in an ammoniacal magnesium mixture; the precipitate after being carefully washed out is decomposed by sodium sulphide, which separates the silver from the uric acid and purin bases as an insoluble sulphide of silver and dissolves the purin bodies. This solution is treated with weak hydrochloric acid, thus separating the uric acid, which crystallizes out after twenty-four hours, leaving the purin bases in solution. The uric acid is then weighed.

For the determination of the purin bases the solution that has been filtered off from the uric acid is treated with an ammoniacal solution of silver, which precipitates the purin bases as purin silver. After washing out this precipitate the silver is determined either by the method of Vohlhard or by ignition and weighing the residue, and thus the amount of the purin bases is determined.

We have omitted to describe all the necessary precautions in this analysis, but one can well imagine what a tedious and long process it is, and, as will be shown later by our experiments, some grave errors are scarcely to be avoided.

Another method of analysis, in view of the facts already mentioned (that the compounds of the purin bodies with silver are definite), is to determine the silver in the precipitate. This method —Haycraft's—is a fairly good one, but, as Huppert says, requires a great deal of skill and precision.

Instead of determining the silver in the precipitate the attempt has been made by Denigès and Czapek to proceed, as above mentioned, with a known amount of silver and to determine the excess of silver in an aliquot part of the filtrate. Denigès used potassium cyanide and Czapek used potassium sulphide. In both methods, and especially the latter, the solution used for titration is unstable and the titre requires to be verified very often. In addition, in the methods of Haycraft, Denigès, and Czapek, the total amount of purin bodies is determined. For the determination of uric acid these methods are not applicable.

Our method is also founded upon the titration of the excess of silver added. It differs from that of Denigès and Czapek in the following respects: For titration we use a solution of potassium

iodide, the titre of which is unchangeable; and, secondly, having by experiments found that silver urate in strong ammonia solutions is insoluble, and that the silver compounds which the purin bases form in the same menstruum are soluble, we are enabled to determine both these bodies by the same procedure.

REQUIREMENTS.

(1) $\frac{N}{50}$ Ag solution.

(2) $\frac{N}{50}$ KI solution.

(3) A nitrous-sulphuric acid mixture.

(4) Starch solution.

(5) NH_4OH. Sp. gr. 0.90.

1 c.c. $\frac{N}{50}$ Ag solution = 0.00336 gr. uric acid = 0.00152 gr. purin base, calculated as xanthin.

The $\frac{N}{50}$ Ag solution is prepared by dissolving 3.3932 grms. $AgNO_3$ previously heated to 120° C. for ten minutes in water, adding 75 c.c. NH_4OH (sp. gr. 0.90) and 10 grms. NH_4Cl and diluting to 1 L. Crystals of pure $AgNO_3$ can be obtained in the market.

The $\frac{N}{50}$ KI solution is prepared by dissolving 3.3200 grms. KI previously heated to 180° C. in water and diluting to 1 L. KI free from iodate, chlorides, and sulphate can be readily obtained.

The nitrous-sulphuric acid mixture is prepared by adding 25 c.c. concentrated H_2SO_4 to 75 c.c. of H_2O and then adding 1 c.c fuming nitric acid.

The $\frac{N}{50}$ solutions are stable, the titre remaining constant after several months, provided the ordinary precautions in preserving silver solutions are observed.

METHOD. *To Determine Uric Acid.* To 110 c.c. of urine add 55 c.c. $\frac{N}{50}$ Ag solution and dilute with NH_4OH (sp. gr. 0.90) to 220 c.c. All these measurements can be conveniently made in flasks of the Giles pattern. Mix and filter through a dry folded filter, either at once or after standing a few minutes. Two portions of 100 c.c., each of which corresponds to 50 c.c. of urine, are collected.

In the mean time a half-dozen small test-tubes (about 8 cm. long and 1 cm. in diameter) are filled for about 1 cm. with a mixture of, roughly, two parts of the nitrous-sulphuric acid and one part starch solution.

To one of the above portions of 100 c.c., $\frac{N}{50}$ KI is rapidly added, and after each addition of 2 c.c. a small portion, not exceeding 0.5 c.c., is removed by means of a pipette, which also answers as a

stirring rod, and carefully introduced down the side of one of the test-tubes in such a manner that two absolutely distinct layers are formed. The end reaction manifests itself sharply by the formation of a blue ring (iodide of starch) at the point of juncture. Having now found the end point approximately with the first 100 c.c., the exact end point is determined with the second 100 c.c.—*e. g.*, say that more than 10 c.c. and less than 12 c.c. are required with the first 100 c.c. The second 100 c.c. are then taken, and 10 c.c. $\frac{N}{50}$ KI run into the solution at once; then a few drops at a time are carefully added, until the exact end point is reached. With a little practice the exact end point can be obtained without having removed more than 1 c.c. from the solution being tested. The entire analysis need not require more than from twenty to twenty-five minutes.

To Determine the Purin Bases. Exactly the same process is carried out except that instead of adding strong NH_4OH we dilute with water—*i. e.*, take 110 c.c. of urine, add 55 c.c. $\frac{N}{50}$ Ag and dilute with water to 220 c.c. and proceed as before. The number of c.c. of $\frac{N}{50}$ Ag used equals the total purin bodies, and, subtracting the number of c.c. of $\frac{N}{50}$ Ag required in the uric acid determination, the difference equals the purin bases. For example:

Determination of Uric Acid.

110 c.c. urine taken; 55 c.c. $\frac{N}{50}$ Ag added; 55 c.c. NH_4OH 0.90 added; 220 c.c. final dilution.

100 c.c filtrate = 50 c.c. urine = 15.9 c.c. $\frac{N}{50}$ KI less 0.3 c.c. correction;

$$25.0 \frac{N}{50} \text{ Ag added} - 15.6 = 9.4 \frac{N}{50} \text{ Ag used.}$$

$9.4 \times 0.00336 = 0.0316$ grm. uric acid in 50 c.c. urine, from which the amount in twenty-four hours is calculated.

Determination of Purin Bases.

110 c.c. urine taken; 55 c.c. $\frac{N}{50}$ Ag added; 55 c.c. water added; 220 c.c. final dilution.

100 c.c. filtrate = 50 c.c. urine = 14.2 c.c. $\frac{N}{50}$ KI less 0.3 c.c. correction = 13.9 c.c.

This 100 c.c. contained 25 $\frac{N}{50}$ Ag added; 11.1 $\frac{N}{50}$ Ag used less 9.4 uric acid Ag = 1.7 purin bases Ag.

$0.00152 \times 1.7 = 0.0026$ grm. xanthin in 50 c.c. urine, from which the amount in twenty-four hours is calculated.

PRECAUTIONS NECESSARY. 1. It is necessary in making the test for iodine that the solutions should be absolutely cold, and it is preferable to place the test-tubes in ice-water.

2. The end reaction can be best observed most accurately in daylight.

3. Many urines, if added to the nitrous-sulphuric acid mixture

and tested by the contact method will develop a reddish-colored ring at the point of contact. This color is due to the action of the acid on the coloring matter of urine, and must not be confounded with the distinctly blue ring produced when iodine is present. The reddish ring becomes apparent only when working with the weak ammoniacal solution, for in the strong ammoniacal solution the AgI precipitates more rapidly, is of a white color and not yellowish, and consequently sets off the blue ring by contrast. If doubt exists as to the nature of the ring it is only necessary to gently shake the test-tube without causing the liquids to mix completely; under these conditions the reddish ring becomes entirely dissipated, whereas the blue iodine ring becomes more distinct.

4. If the relationship of the standard solutions is determined under the same conditions as those under which the analyses with urine are carried out, it will be found that 0.3 c.c. more of the $\frac{N}{50}$ KI will be required to develop the end reaction than the number of c.c. of $\frac{N}{50}$ Ag used. This is owing to the fact that there is a limit to the delicacy of the test for iodine, and that it is necessary to add 0.2 c.c. $\frac{N}{50}$ KI to 100 c.c. H_2O in order that 0.5 c.c. of this dilution should give the reaction for I. When we remember that this 0.5 c.c. contains only 0.00332 mgr. of KI the extreme delicacy of the end reaction as performed by the contact method is appreciated.

Rogovin[1] has recently shown that the $HNO_2 + H_2SO_4$ test is the most delicate test for I. We came to this same conclusion independently, but found that by the contact method we could increase the delicacy of the reaction to a marked degree. The $\frac{N}{50}$ Ag and $\frac{N}{50}$ KI should therefore be standardized, using approximately the same dilution (100 c.c.) as in the analysis of urine, and the necessary correction obtained, which will be 0.3 to 0.4 c.c. if the solutions have been accurately prepared.

In order to prove the accuracy of our method in determining both uric acid and the total purin bodies, the following points were established experimentally:

1. That the Ag compound formed with uric acid under the conditions stated is insoluble both in dilute and in strong NH_4OH solutions.

2. That the Ag compound formed with the purin bases under the conditions stated is insoluble in weak ammoniacal solution and soluble in strong NH_4OH.

3. That known amounts of uric acid, when added either to water alone or to urine, can be accurately determined. This was shown

[1] Berliner klin. Wochenschr., 1903, S. 863.

to be the case under varying conditions and with uric acid from various sources.

4. That the uric acid determinations agree with determinations made by the Ludwig-Salkowski method.

5. That the determinations of the total purin bodies agrees with the results obtained by Arnstein's modification of Camerer's method.

6. That Ag can be determined with great accuracy by means of KI in an ammoniacal solution.

We shall in a separate paper publish a comparison of the accuracy of this means of determining silver as compared with other volumetric methods.

EXPERIMENTAL PART. (1) *With Uric Acid.* The uric acid which was used was obtained from three sources: two were commercial products and one was obtained from urine. The purity of one of the commercial products (A) was established by nitrogen (Kjehldal) determinations, as follows:

	Per cent.	
	Found.	Calculated.
0.0814 gr. yielded 0.0269 gr. N	33.06	33.33
0.0952 gr. yielded 0.0316 gr. N	33.20	

The second commercial product (B) was purified by recrystallization and the uric acid from urine (C) was purified by washing with alcohol and repeatedly recrystallizing till an almost colorless product was eventually obtained.

Solubility of the Precipitate which Uric Acid Forms with an Ammoniacal Solution of Silver Containing Ammonium Chloride. 0.100 gr. of uric acid (A) was dissolved in 10 c.c. of a cold saturated solution of $LiCO_3$ and diluted to 100 c.c. This solution is designated "D." The solubility was determined both in water and in urine. A urine free from all purin bodies was prepared by precipitating these bodies by means of Salkowski's ammoniacal silver solution and then adding only enough NH_4OH to dissolve the AgCl formed. In each case the final dilution was 50 c.c., and this contained 2 c.c. of the $\frac{N}{50}$ Ag solution.

Solubility in Water.

Solution "D" added . .	1.00 c.c.	0.5 c.c.	0.25 c.c.
Uric acid	1.00 mg.	0.5 mg.	0.25 mg.
Corresponding to 1 part in	50,000	100,000	200,000
Result	Marked precipitate.	Slight precipitate.	Very slight precipitate, readily noticeable on standing eighteen hours.
	Containing 25 per cent. NH_4OH.		Sp. gr. 0.90.
Solution "D" added . .	1.00 c.c.	0.5 c.c.	0.3 c.c.
Uric acid	1.00 mg.	0.5 mg.	0.3 mg.
Corresponding to 1 part in	50,000	100,000	167,000
Result	Slight precipitate.	Very slight precipitate which collects after eighteen hours.	Turbidity which settles as a precipitate after eighteen hours.

Solubility in a Purin-free Urine.

Solution "D" added . .	1.0 c.c.	0 5 c.c.	0.25 c.c.
Uric acid in	1.0 mg.	0.5 mg.	0.25 mg.
Corresponding to 1 part in	50,000	100,000	200,000
Result	Marked precipitate.	Precipitate.	Slight precipitate.
	Containing 25 per cent. NH_4OH.		Sp. gr. 0.90.
Solution "A" added . .	1.0 c.c.	0.5 c.c.	0.25 c.c.
Uric acid in	1.0 mg.	0.5 mg.	0.25 mg.
Corresponding to 1 part in	50,000	100,000	200,000
Result	Precipitate.	Slight precipitate.	Turbidity which settles as a precipitate in eighteen hours.

The results show that in urine, whether in a weak or strong ammoniacal solution, the silver urate precipitate is less soluble than 1 part in 200,000; or, in other words, so slight as to be negligible. The same is practically true of aqueous solutions.

Solubility of the Silver Precipitate Formed by the Purin Bases in NH_4OH in the Presence of Urine. The purin bases were separated from 1000 c.c. of urine according to the method of Salkowski.[1] The acid solution (E) containing these bases, which probably also contained a trace of uric acid, was diluted to 100 c.c.

A urine from which all the purin bodies had been removed was used in making the following tests:

Twenty c.c. of solution E containing the purin bases were added to 200 c.c. of the purin-free urine (F). A small quantity of $\frac{N}{50}$ Ag solution was then added and a voluminous precipitate obtained. The same experiment was repeated, except that enough NH_4OH of specific gravity 0.90 was added to form 25 per cent. of the final dilution. Under these conditions instead of a voluminous precipitate being formed, only a slight turbidity was produced, thus proving that the purin bases are practically entirely held in solution in an NH_4OH solution of this strength, and are perhaps entirely soluble, since the turbidity obtained was in all probabliity caused by the trace of uric acid which the solution used contained.

In the presence of solutions containing less than 25 per cent. NH_4OH, the purin bases are progressively less soluble. The same results have been obtained in control experiments. Moreover, it is a fact that although the precipitate of the Ag compound can readily be prevented if sufficient NH_4OH be present, it is much more difficult to dissolve this precipitate if once formed in a weak NH_4OH solution, even though strong NH_4OH is then added in large excess.

Determination of Uric Acid in Aqueous Solutions. In the following experiments the commercial uric acids "A" and "B" and

[1] Pflüger's Archiv, 1898, Bd. lxix. p. 280.

the uric acid from urine "C" were used as indicated. As a rule, the uric acid was dissolved in 15 to 20 c.c. of a saturated solution of $LiCO_3$ in the cold. In a few instances Na_2CO_3 was used, in which cases the solution was slightly warmed.

Fifty-five c.c. $\frac{N}{50}$ Ag were invariably added. In some cases which are indicated the precipitation was made in the presence of 55 c.c. NH_4OH, specific gravity 0.90. The final dilution was always 220 c.c., and the determinations were made in two portions of 100 c.c. each.

Number of experiment.	Source of uric acid used.	Total uric acid dissolved.	Solvent used.	$\frac{N}{50}$ Ag required for 100 c.c.	Uric acid found.	Uric acid added.
1	A	0.1133 gr.	$LiCO_3$	15.3 c.c.	0.0514 gr.	0.0515 gr.
2	A	0.1110 "	"	14.8 "	0.0497 "	0.0505 "
3	A	0.1007 "	"	14.1 "	0.0474 "	0.0458 "
4	A	0.1248 "	"	17 3 "	0.0581 "	0.0567 "
5	A	0.1003 "	"	13 7 "	0.0460 "	0.0456 "
6	A	0.1200 "	"	16.6 "	0 0556 "	0.0545 "
7	B	0.0517 "	Na_2CO_3	7.1 "	0.0238 "	0.0235 "
8	B	0.1057 "	$LiCO_3$	14.1 "	0.0474 "	0.0480 "
9	B	0.1255 "	"	16.8 "	0.0564 "	0.0570 "
10	C	0.0908 "	Na_2CO_3	12.0 "	0.0403 "	0.0412 "
11	B	0.1098 "	$LiCO_3$	14.6 "	0.0491 "	0.0499 "
12	B	0.1015 "	"	13.4 "	0.0450 "	0.0461 "

In No. 11 and No. 12 precipitation was made in the presence of 25 per cent. NH_4OH, specific gravity 0.90.

The uric acid "A," as previously indicated, was not a recrystallized product, which probably accounts for the slight plus error found in several instances.

Determination of Uric Acid Dissolved in a Urine from which the Purin Bodies had been Previously Removed. The purin bodies were removed from a urine by adding Salkowski's Ag solution in excess and sufficient NH_4OH to dissolve all AgCl. After filtering the urine was acidified with HNO_3, allowed to stand, and the AgCl filtered off. In order to confirm the fact that the urine now contained neither purin bodies nor silver, a definite quantity of $\frac{N}{50}$ Ag solution was added, and this titrated with the $\frac{N}{50}$ KI under the exact conditions in which the following analyses with definite quantities of uric acid were made, with the result that the correct agreement in the titre was found.

The uric acid "A" was invariably dissolved in 10 to 20 c.c. of a saturated solution of $LiCO_3$ in the cold; 55 c.c. $\frac{N}{50}$ Ag solution were then added, followed by about 90 c.c. of the purin-free urine and 55 c.c. NH_4OH, specific gravity 0.90. The solution was diluted finally to exactly 220 c.c. with the same urine. The solution thus contained 25 per cent. of strong NH_4OH. As usual, two portions

of 100 c.c. each were filtered off and the determinations made with these two solutions.

Number of experiment.	Total uric acid dissolved.	$\frac{N}{50}$ Ag required.	Uric acid found in 100 c.c.	Uric acid added in 100 c.c.
1	0.1095	14.7	0.0494	0.0498
2	0.1006	13.5	0.0456	0.0457
3	0.1030	14.0	0.0471	0.0468
4	0.1290	17.3	0.0581	0.0586
5	0.0824	11.2	0.0376	0.0375
6	0.1021	13.6	0.0457	0.0464
7	0.0595	7.9	0.0265	0.0270

No. 7 was a uric acid from urine.

Comparison of the New Method with the Ludwig-Salkowski Method. The Ludwig-Salkowski method has by common consent been accepted as the standard method for determining uric acid in urine. The method, however, is far from being an ideal one aside from the time factor. Leaving out of account entirely minor errors for which corrections can be made, or which with care may partially be avoided, there are, in addition, certain gross errors which can materially affect the results obtained.

Geelmuyden[1] has shown in a series of fourteen determinations that invariably a lower result is obtained by making nitrogen determinations on the uric acid as eventually separated in the course of the method than by weighing the precipitate. The differences in the two procedures amounted to as much as 22.4 per cent. in one case, and the average difference found was 9.3 per cent. It is true that Geelmuyden weighed the uric acid in the objectionable paper filter and did not remove the sulphur from the precipitate, yet these points alone do not account for the marked discrepancy found.

Again, the Ludwig-Salkowski method depends upon a weak HCl solution to finally separate the uric acid from the purin bases.[2] It is, however, a fact[3] that both xanthin and guanin are soluble with difficulty even in strong HCl, consequently in a urine which contains these substances in comparatively large amounts the uric acid thus separated will be contaminated by them and the result vitiated to this extent.

In the following analyses the Ludwig-Salkowski method was followed as described in Huppert's work. One modification was made in regard to the final weighing of the uric acid.

It was our experience that instead of it being the exception that Ag_2S should separate with the uric acid, this was rather the rule; moreover, the amount was quite appreciable. Thus, in two cases in which the amount was determined, we found 7.9 mg. and 11.1 mg. To remove this Ag_2S by means of alkali hydrate, as has been

[1] Zeitsch. f. Analyt. Chem., 1892, 31, 160.

[2] Salkowski's Pract., S. 251.

[3] Huppert in Neubauer und Vogel Analyse des Harns, 1898, pp. 338, 344, 350.

proposed, would introduce as great an error by the decomposition of the uric acid as the one it was intended to correct. For this reason, acting upon the advice of Dr. E. E. Smith, we collected the uric acid in a Gooch crucible, and after drying to constant weight ignited and calculated the uric acid by the loss in weight. Although by this means we do not entirely eliminate the error due to contamination by Ag_2S, since the sulphide is converted into oxide, still the error is reduced to a minimum.

In the following analyses it will be seen that in most cases the agreement between the Ludwig-Salkowski method and the new method is close, but that in some cases considerably more uric acid is found by the Ludwig-Salkowski method. This, we believe, is due to the fact, as pointed out above, that in the Ludwig-Salkowski method the uric acid can easily become contaminated by some of the more insoluble purin bases, should these be present.

In each case 100 c.c. were used in carrying out the Ludwig-Salkowski method. The new method was followed as previously described.

Analysis number.	Uric acid by new method in 100 c.c.	Uric acid by Ludwig-Salkowski method in 100 c.c.	Description of urine used.
1	0.0598 gr.	0.0609 0.0612	Normal.
2	0.0437 "	0.0436	Normal of pregnancy.
3	0.0504 "	0.0506	Normal of pregnancy.
4	0.0961 "	0.0964 0.0992	Leukæmic.
5	0.1015 "	0.1040 0.0994	Leukæmic.
6	0.0745 "	0.0758	Enteric fever.
7	0.1008 "	0.1027	Tubercular pneumothorax.
8	0.0658 "	0.0744 0.0701	Normal.
9	0.0370 "	0.0413	Leukæmic.
10	0.0631 "	0.0687	Normal.

DETERMINATION OF THE TOTAL PURIN BODIES. *Comparison of the New Method with Arnstein's Modification of Camerer's Method.*[1] In this method the purin bodies are determined by making nitrogen (Kjehldal) determinations on the silver precipitate, care having been taken to remove the last traces of NH_4OH from the precipitate by boiling it with water and magnesia. In the following analyses the total purin bodies were calculated as uric acid.

A comparison of the results obtained based on the uric acid is sufficiently accurate for all practical purposes. Since, however, in the one case we calculate the uric acid from the N content, and in the other case from the Ag content, a strictly accurate comparison is impossible, in view of the fact that we are dealing with a heterogeneous mixture.

[1] Zeitsch. f. Physiol., 1897, Ch. 23, 426; Med. Wissensch., 1898, 15, 257.

Number of analysis.	Total purin bodies by Arnstein's modification of Camerer's method in 100 c.c. urine.	Total purin bodies by new method in 100 c.c. urine.
1	0.0816 gr.	0.0846
2	{0.0777 / 0.0787} "	0.0793
3	0.0814 "	0.0852
4	{0.0651 / 0.0661} "	0.0665

Determination of the Total Purin Bodies in Urines to which Known Amounts of Uric Acid had been Added. The total purin bodies were determined in a urine by the new method as previously described, and the result calculated as uric acid.

To 110 c.c. of the same urine a definite quantity of uric acid dissolved in a cold saturated solution of $LiCO_3$ was then added, the purin bodies precipitated by 55 c.c. $\frac{N}{50}$ Ag solution, and the final dilution brought up to 220 c.c. with water. The determinations were then made as before in two portions of 100 c.c. each, and the results calculated as uric acid.

Experiment number.	Purin bodies in 50 c.c. urine.	Uric acid added to this urine.	Total purin bodies found in 100 c.c.	Uric acid actually added to 100 c.c.	Uric acid found.
1	0.0302	0.0922	0.0736	0.0419	0.0424
2	0.0302	0.0823	0.0675	0.0374	0.0374
3	0.0356	0.0752	0.0708	0.0342	0.0352

No. 3 contained uric acid obtained from urine.

In conclusion, we will call attention to the following points: We found that a few drops of chloroform added to urine will prevent decomposition of the purin bodies. In several instances a urine to which chloroform had been added gave the same result after standing seventy-two hours as was obtained originally.

If the urine contains a uric acid deposit this should be brought into solution either by warming, or, what will usually be found necessary, by dissolving this deposit in a small quantity of a saturated solution of $LiCO_3$.

If a urine contains KI this must be removed by adding $AgNO_3$ in excess and then a chloride to remove the excess of Ag.

Albumin and sugar apparently exert no deleterious influence.

The method as proposed deserves the designation of "a clinical method" in the sense that it places at the disposal of the clinician an accurate method for the determination of both the total purin bodies and the uric acid, determinations that can be made in a short period of time—far shorter than by any of the numerous other methods that have been proposed. On the other hand, the term "clinical method" is looked upon by chemists, not without good reason, as a term indicating a method grossly inaccurate, and in this sense the method does not deserve to be known as a clinical method.

THE VASOMOTOR FACTOR IN THE CLINICAL MEASUREMENT OF THE BLOOD PRESSURE.[1]

By Albert Abrams, A.M., M.D.,
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In this contribution specific reference will be made to blood pressure observed in arteriosclerosis. To me one of the most paradoxical manifestations of arteriosclerosis is the pronounced high blood pressure coupled with the local evidence of cardiac incompensation. The latter refers specifically to the enfeebled heart revealed by cardiac auscultation. In other words, the cardiac tones are weak, whereas the blood pressure is relatively high. In his studies in stethophonometry[2] the writer was better able to appreciate the foregoing fact than he would be were he guided by the conventional method of cardiac auscultation. The stethophonometer is a little piece of mechanism with coarse and fine adjustment attachable to the stethoscope containing a composition material which offers gradual increasing resistance to sound. The stethophonometer demonstrates that the intensity of the heart tones is no accurate gauge of heart strength. The instrument in question enables one to differentiate the muscular and valvular components of the heart sounds, and serves further to distinguish murmurs of valvular and muscular genesis.

Another important aid furnished by the instrument is in recognizing organic from inorganic cardiac murmurs and autochthonous from transmitted murmurs. Elsewhere[3] the writer has referred to inhibition of the heart as an aid in diagnosis. This manœuvre took into consideration the fact that the intensity of a cardiac murmur was dependent on the vigor of the heart. Loud murmurs often become weak or disappear in the course of febrile affections and in the moribund state owing to the slow and feeble action of the heart. The expedient in question seeks to slow the action of the heart, and in its execution we are constrained to rely on the efforts of the patient. This is not necessary if the stethophonometer is employed. By interposing increasing resistance to transmission inorganic and transmitted murmurs may be made to disappear to be replaced by tones. The stethophonometer has taught the writer that the unreserved reliance placed on the tonometer and other instruments for gauging blood pressure in arteriosclerosis is unwarranted by clinical evidence. It is usually taught that when the

[1] Read by invitation before the Oregon State Medical Association, Portland, Oregon, August 30, 1904.

[2] Abrams. Diseases of the Heart, 1900, p. 169; Medical News, July 8, 1899; New York Medical Journal, October 18, 1902.

[3] Philadelphia Medical Journal, September 29, 1900.

tonometric figure is low, with clinical evidence of arteriosclerosis, it is a sign of failing heart power. The tonometer and other like apparatus are constructed on the general principle that, after the blood supply to a part is inhibited by compression, the gradual removal of the latter will relieve the obstruction, and, when the point is attained at which the intra-arterial is greater than the extra-arterial or capillary pressure, it is indicated by a gauge which registers the blood pressure.

Now, in arteriosclerosis even the smallest bloodvessels (arterio-capillary fibrosis) are firm and unyielding, hence the compression of such vessels for gauging blood pressure conduces to erroneous results. Three factors make up the normal blood pressure, viz., force of the ventricle, frictional resistance of the capillaries, and arterial elasticity.

If the heart is weak, as is manifested by an enfeebled second aortic tone, increased blood pressure can never indicate a vigorous heart action, as is currently supposed. I am, therefore, constrained to conclude that in estimating the vigor of the myocardium blood pressure is of subsidiary value only and then when coupled with cardiac auscultation. There is unquestionably a vasomotor factor concerned in the maintenance of high blood pressure when cardiac enfeeblement coexists. I fully realize that I am running counter to orthodox teaching when I assume the contention that relatively high blood pressure is the necessary corollary of a weak heart. Compensation in cardiac anomalies is not necessarily confined to an increased capacity for work of the heart musculature, for there are many other compensatory factors, as, for instance, the augmentation of vascular tone in mitral stenosis and the diminution of the same tone in aortic regurgitation. We are in a position to estimate the degree of myocardial insufficiency, but the sufficiency of vasomotor and nerve influences in maintaining the circulation has heretofore baffled the efforts of clinical interpretation. Whereas, it is true that augmented peripheral resistance represented by increased function of the vasomotor nerves calls forth the latent energy of the heart, such increase in energy is fully compensated by the diminution in the number of heart beats. In general, increased blood pressure denotes a diminished and lowered blood pressure, an increased frequency of the pulse. One cannot gainsay that of the two conditions, increased blood pressure and increased energy of the heart, the former is preferable.

The blood supply to the heart occurs during diastole, and inasmuch as an increased pulse rate is at the expense of diastole, the nutrition of that organ must necessarily suffer. The nutrition of the heart is dependent on the pressure in the aorta, and when this sinks less blood is propelled into the coronary arteries. Such is the inconsistency of the average practitioner that, while he looks askance at high blood pressure and endeavors to subdue it, he does not

hesitate to goad the heart by cardiotonic medication. Increased peripheral resistance of the bloodvessels serves as a prop to the enfeebled heart. We are inclined to forget that the elastic reaction of the arterial walls is an important factor in aiding the circulation of the blood, in fact, the arterial system is a subsidiary heart.

A rigid artery even in early arteriosclerosis is of no earthly benefit to its possessor; indeed, it is an incumbrance, yet that very artery may be made to yield its modicum of duty by augmented activity of the vasomotor system of nerves which puts it in a condition of moderate contraction. Thus the nervous system may compensate an impaired myocardium. That the bloodvessels are by no means a subordinate factor in furthering the circulation is evidenced by the recent observations of Hasebroek.[1] This writer tentatively proclaims a new theory based on the fact that there is a propulsive energy at the periphery independent of that in the heart, and that the periphery represents another second independent pumping apparatus, coupled with that of the heart. The periphery has not only its elastic contraction and expansion, but also its active diastole and systole in the arteries. This diastolic systolic activity is manifested in the capillaries as a sucking-in, an inspiration, as it were, while in the arteries it is more of a propulsive energy. Both these forces combine to create an independent and forcible stream into the veins which are passive and merely serve as a passive reservoir for the blood stream.

It is generally conceded that all of the factors that make up blood pressure the resistance offered by the bloodvessels is paramount. If the vessels are dilated, the pressure falls; if contracted, it will rise.

The nervous mechanism which presides over the tonus of the bloodvessels is the vasomotor apparatus, and while the latter I concede may be reflexly influenced by irritation from the bloodvessels themselves or from the end organs of sensory nerves in general, we are inclined to forget that the vasomotor apparatus may operate independently of such influences. Emotions and the state of the mind in general greatly influence the calibre of the bloodvessels through the vasomotor system of nerves. Take neurasthenics for a paradigm, and I have examined a large number of them at different periods under emotional influences, intense mental application, and when their brains were at rest, and in each instance my results varied. Emotional influences and intellectual application increased blood pressure, while mental rest reduced it. Again, increased cardiac pressure does not react equally on all the bloodvessels, and this is evidenced by the fact that the blood pressure in both radials is not always the same. Physical activity, the ingestion of food, menstruation, and other conditions also modify blood pressure. Another and more important factor influencing blood

[1] Deutsche Archiv f. klin. Med., Berlin, Bd. lxxvii. Nos. 3 and 4.

pressure is the heart volume, which is continually subject to reflex conditions. The writer has repeatedly demonstrated the occurrence of the *heart reflex* as a result of nasal and gastric irritation as well as by irritation of the skin over the precordial region. The writer's heart reflex has been repeatedly confirmed notably by Merklen and Heitz[1] and Heitler.[2]

The writer has recently demonstrated also a heart reflex of dilatation, aortic reflexes and myopathic and psychic heart reflexes,[3] facts which still further suggest variations in heart volume and changes in blood pressure. Without entering further into a discussion of these preliminary facts we may at once proceed to determine if possible how the clinical vasomotor factor may be excluded in estimating the blood pressure. In the following investigations the Riva-Rocci instrument was employed in gauging blood pressure. After the blood pressure was determined according to the customary method, the patient was instructed to inhale nitrite of amyl from a bottle, after which procedure the blood pressure was again estimated, and the difference noted. The arm-piece of the instrument need not be removed until the investigations are completed.

It is wise to instruct the patient not to practice forced breathing while inhaling the amyl nitrite, as observation has taught me that this physiologic act will reduce blood pressure and thus negative the clinical findings. . Sufficient of the drug must be inhaled to induce the physiologic action, viz., slight duskiness of the face, fulness in the head, and relaxation of the bloodvessels. A few words noted elsewhere[4] are here apposite with reference to the physiologic action of the drug.

Amyl nitrite will intensify feeble cardiac murmurs, but ordinarily it is not serviceable in diagnosis, owing to the creation of cardiomuscular murmurs, which have no reality other than in the delirious state of the organ.

To bring out aneurysmal pulsations while the x-rays are traversing the chest, it is indispensable, although the aortic reflexes are more available in this regard.

During the inhalation of amyl nitrite in a certain percentage of persons the transverse diameter of the heart will become diminished. This drug is almost a specific in inhibiting the distress of angina pectoris, and if it reduces the cardiac area as the writer has demonstrated, the theory of Heberden, that angina pectoris is a cramp of the heart muscle, must be wrong. The theory of extreme tension of the ventricular walls in consequence of acute dilatation seems to be corroborated by the action of the drug upon the heart.

I have observed another phenomenon associated with the inhala-

[1] La presse médicale, August 1, 1903.
[2] Wiener klin. Wochen., 1890; and Centralbl. f. d. ges. Therapie, 1893.
[3] American Medicine, January 3, 1903.
[4] Ibid., July 16, 1904.

tion of amyl nitrite, and that is a limited patch of dulness which develops over the manubrium sterni.

This patch of dulness may involve the entire manubrium and extend to the right as well as to the left side. The dulness in question is almost never reproduced after an immediate second inhalation of the drug. The dulness is caused by circumscribed collapse of lung (the lung reflex of contraction). In some persons inhalation of the drug evokes dull areas in other chest regions, but the manubrium dulness is practically constant. The latter area of dulness may at once be dissipated by tapping the epigastrium, which provokes the counter lung reflex of dilatation. In the following table the blood pressure of ten average normal individuals is presented showing the influence on blood pressure after inhalation of amyl nitrite during the time that the face of the patient was flushed, the latter being in the sitting posture:

Case.	Age.	Blood pressure before and after inhalation of amyl nitrite. Before.	After.
1	10	115 mm.	125 mm.
2	13	125 "	145 "
3	20	133 "	140 "
4	20	140 "	143 "
5	25	135 "	139 "
6	19	128 "	128 "
7	33	148 "	150 "
8	25	134 "	142 "
9	27	158 "	160 "
10	36	153 "	165 "

In the foregoing table one notes that the average effect of amyl nitrite inhalation in the normal individual is to cause a slight in-increase of blood pressure.

One may also observe in the examination of the normal individual that the primary effect of the inhalation is to slightly depress the blood pressure, but it rises at once. I am inclined to conclude that in the average healthy person the inhalation of amyl nitrite relaxes the arterial wall by elimination of the vasomotor influence, thus bringing into play the veritable cardiac pressure.

An examination of many arteriosclerotics after the foregoing procedure prompts me to classify them as follows:

1. Arteriosclerotics with high blood pressure and strong cardiac tones who show after inhalation of amyl nitrite a stabile or a slight rise of blood pressure, as is demonstrated by the selection of the following subjects:

Case.	Age.	Blood pressure before and after inhalation of amyl nitrite. Before.	After.
1	62	157 mm.	163 mm.
2	68	210 "	210 "
3	58	160 "	165 "
4	60	168 "	168 "
5	64	174 "	176 "

2. Arteriosclerotics with high blood pressure and enfeebled cardiac tones, who show after the inhalation a decided decrease of blood pressure. In these as well as in the succeeding class the reduction in blood tension was no doubt influenced by the elimination of the tonus of the arteries, which was maintained by the vasomotor system of nerves, thus allowing the true endocardial pressure, which was enfeebled, to be brought into action.

Case.	Age.	Blood pressure before and after inhalation of amyl nitrite.	
		Before.	After.
1	74	218 mm.	190 mm.
2	59	240 "	195 "
3	62	200 "	175 "
4	71	210 "	180 "
5	60	290 "	240 "

3. A final class of patients with arteriosclerosis with relatively low blood pressure and enfeebled heart tones who demonstrate a still further reduction of blood pressure after inhalation of amyl nitrite, as the following table shows:

Case.	Age.	Blood pressure before and after inhalation of amyl nitrite.	
		Before.	After.
1	53	125 mm.	115 mm.
2	60	120 "	115 "
3	65	150 "	125 "
4	70	130 "	120 "
5	61	135 "	130 "

In a prognostic sense the patients in the last class belong to the hopeless category, insomuch as the vasomotor system of nerves is either exhausted or unable to properly usurp the functions of a failing heart.

Desirous of determining the influence of digitalis on some of the preceding cases, I have selected from the second class of arteriosclerotics Cases I. and V. and from the third class Cases II., IV., and V. A tablespoonful of a reliable infusion of digitalis was administered three times a day for five days, when it was presumed that the digitalis had brought about its physiological effects, and the following results were attained:

Class.	Case.	Blood pressure after using	
		Digitalis.	Amyl nitrite.
2	1	215 mm.	150 mm.
2	5	240 "	200 "
3	2	160 "	130 "
3	4	140 "	130 "
3	5	140 "	135 "

Digitalis is the sovereign heart tonic, and is correctly specified as the quinine of the heart. All heart tonics are divided into direct and indirect: the former acting by direct stimulation of the heart, the latter by improving the nutrition of the organ or by relieving vessel tension hastening the output of blood from the heart.

The digitalis substances in the therapeutic stadium have a dual action by slowing the pulse and augmenting the blood pressure. The latter is the product of two forces, viz., increased heart work and augmentation of the vessel tone.

The action on the heart of the digitalis substances is to increase the work of both ventricles, but in not a few instances increased work on the part of the left ventricle signifies an increased blood pressure which is very often an undesirable condition, as in nephritides and arteriosclerosis. It is usually taught that high blood pressure as in arteriosclerosis is a contraindication for the administration of digitalis, although Sahli[1] has demonstrated that in conditions of stasis with increased peripheral resistance digitalis possesses a paradoxical action, insomuch as it combats the stasis and reduces the blood pressure. Some of the theories established for the purpose of creating indications and contraindications for the administration of digitalis suggest the comment of the mathematician, who, having demonstrated a new mathematical theory, thanked God that it could not be of the slightest utility to any living soul. Many of the theories in question also remind me of the erudite German professor of economics who received a bed as a present. Until the small hours of the morning he busied himself with abstruse calculations to determine whether he was large enough for the bed or if the latter were large enough for him. Finally, he was struck with the happy idea of getting into the bed, and to his intense delight discovered that it was admirably suited to his proportions.

So it is with digitalis; this valuable cardiotonic is often relegated to oblivion owing to the numerous theories which indicate and contraindicate its employment.

No theory can guide the practitioner in the use of digitalis, and its tentative administration is always warranted, provided the physician begins with small doses and is prepared to recognize its untoward effects.

I have never permitted the high blood pressure nor the tortuous arteries in arteriosclerosis to thwart me in the use of digitalis, and my temerity, if it may be so specified, has rarely guided me into error. Very true, my conception of blood pressure in arteriosclerosis may be heterodoxical, and it is perhaps for this very reason that I have ignored the circumspection of the doctrinaire.

The cases cited in the table showing the effects on blood pressure after the use of digitalis may serve as a vehicle for my contention. In Class 2, Case I., the blood pressure before using digitalis was 218 mm., and after inhalation of amyl nitrite it was reduced to 190 mm.

After the use of digitalis it was 215, but the inhalation of amyl nitrite reduced it to 150 mm. Now, the theory of action of the drug on the patient is practically as follows: The blood pressure was essentially the same after as before the use of digitalis, but while

[1] Verhandl. d. XIX. Kongr. f. innere Med.

amyl nitrite before the use of digitalis reduced the blood pressure only 28 mm., after its use the pressure was reduced 65 mm. This indicated that the digitalis was unfavorable in its action, for, after the tonus of the bloodvessels was removed by amyl nitrite the greater reduction in blood pressure demonstrrated the cardiac force was further reduced after than before the use of digitalis. In other words, digitalis was goading a jaded heart, and the high blood pressure was illusory. This action is not uncommon in the administration of digitalis, owing to its vasoconstrictor influence, and when the latter action implicates the coronary bloodvessels the nutrition of the heart must suffer. In such instances, in determining the action of digitalis, we must often decide whether prolongation of the diastole can compensate for the defective nutrition.

In the case last cited the action of digitalis was unfavorable, but when it was given in combinatiom with *diuretin*, which seems to antagonize the vasoconstrictor components of digitalis, the action of the latter drug was more favorable, the blood pressure falling only 15 mm. in lieu of 65 mm.

This combination of diuretin with digitalis in arteriosclerosis is more often advantageous than the combination of the latter drug with nitroglycerin. Very frequently the use of a brisk purgative in arteriosclerosis—*e. g.*, a combination of calomel and jalap for the purpose of unloading the bloodvessels—will be productive of more good than anything else, and will also further the action of digitalis and other cardiotonics. Whereas, the degree of passive hyperæmia of the lungs may be regarded as a gauge of the functional capacity of the right heart ventricle so, also, may the size of the liver be utilized as a guide of venous stasis, for the latter organ is practically a reservoir for the right ventricle. Even in the early stages of cardiac insufficiency the liver enlarges, whereas in the later stages the systolic liver pulse indicates that a tricuspid insufficiency has been added to dilatation of the right ventricle.

What I have called the cardiosplanchnic phenomenon serves a useful purpose in determining the grade of congestion in the splanchnic area. This phenomenon is based on the experimental investigations of Hill and Barnard,[1] who demonstrated that there is a tendency for the blood to accumulate in the splanchnic area, and that the great splanchnic veins are very susceptible to pressure, and that a large quantity of blood may be squeezed out of them by firm compressions of the belly with the hand. If a series of firm abdominal compressions with the hand are made in the average individual and the lower sternal region—*i. e.*, the part of the sternum contiguous to the heart is percussed—a pronounced dulness or even flatness will have been found to supersede the normal resonance.

The dulness in question is at once dissipated by a series of deep breaths. This is the cardiosplanchnic phenomenon, and is depend-

[1] Abrams. Splanchnic Neurasthenia, 1904, p. 171, and THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, January, 1904.

ent on the fact that by abdominal compression blood is expressed from the splanchnic veins to the right heart. In some individuals the phenomenon is but feebly expressed, and its degree of expression is proportional to the grade of congestion of the splanchnic veins. If in arteriosclerosis, splanchnic congestion is pronounced digitalin or strophanthin alone or in combination are especially indicated. They are endowed with the property of constricting the splanchnic vessels alone, whereas digitoxin exerts its vasoconstrictor influence on all the bloodvessels. In the action of digitalin and strophanthin we possess a cogent means of relieving the burden of the heart by increasing the receptivity of the peripheral bloodvessels for the blood which has been expressed from the abdominal organs, and the same agents are almost specific in action in relieving splanchnic congestion, which is the underlying condition in splanchnic neurasthenia. For relieving splanchnic congestion the abdominal application of the sinusoidal current is paramount. A few words may be permitted with reference to the action of amyl nitrite. With this drug there is frequently an idiosyncrasy expressed; the subjects are either abnormally susceptible or refractory to its physiological action. In two instances following its inhalation the writer noted a veritable inhibition of the heart and absence of the pulse. The writer recalls a previous statement, viz., that the inhalation of amyl nitrite causes a reduction in the heart volume which is tantamount to a heart reflex, and in the two subjects just cited during the time the drug was inhaled with the *x*-rays traversing the chest the reduction in the heart volume was very much exaggerated above the normal.

A pertinent example of autosuggestion is afforded in one instance from the inhalation of amyl nitrite.

The subject, who had taken chloroform for an operation a few months before, contended while inhaling amyl nitrite that I was giving him chloroform, and in a minute or two he passed into a condition of narcosis, during which time he proved insusceptible to the infliction of pain.

This example of autosuggestion is somewhat analogous to that occurring in the practice of a well-known chloroformist who had occasion to give ether to an hysterical girl who was about to have two small scalp tumors removed.

He found that the ether bottle was empty, and while waiting for a new supply to be brought he instructed the patient how to take deep breaths. After a few deep inspirations she cried, "I am going off," and became unconscious. Both tumors were painlessly removed in this state. It was subsequently learned that the girl had taken ether once before, and the association of ideas merely recalled the effects of ether.

The writer formulates the following conclusions:

1. That blood pressure is an expression of action of two chief factors: ventricular force and vasoconstriction.

2. The inhalation of amyl nitrite will dissipate the vasoconstrictor factor and bring into play the ventricular force, which is the real factor to be encouraged in a failing heart.

3. The vasoconstrictor factor may and does compensate ventricular inadequacy, for it is essential in most cardioarterial diseases for the blood pressure to be maintained to afford better nutrition for the heart and to promote arterial elasticity as a means of establishing the circulation of the blood.

4. The recognition of the ventricular and vasomotor factors in blood pressure serves as a clue in the correct administration of cardiotonics.

5. In the individual endowed with cardiac health the removal of the vasomotor factor causes an increase in blood pressure, whereas the converse condition causes the latter to fall, and the degree of reduction is proportional to the degree of cardiac enfeeblement.

6. The execution of the foregoing manœuvres in estimating heart vigor is by no means comparable to a correct method of cardiac auscultation, although the latter method does not indicate how much of the cardiac force may be attributed to increased peripheral resistance. Cardiac auscultation in conjunction with the sphygmomanometer and the inhalation of amyl nitrite constitute the ideal methods for eliciting the real condition of things.

7. In estimating blood pressure the sphygmomanometer only gauges the force of the left ventricle, and to determine the sufficiency of the right ventricle auscultation of the pulmonic sounds and a physical examination of the lungs are alone adequate.

8. There are certain individuals in whom one finds high blood pressure without cardiac weakness, and after inhalation of amyl nitrite the blood pressure remains the same. Such cases are associated with traces of albumin in the urine, which is of low specific gravity, and are practically instances of incipient chronic interstitial nephritis.

9. It is evident that persistent high blood pressure dependent on augmented tonus of the vasomotor centre is a cogent etiological factor in arteriosclerosis independent of any other cause, and is merely the reaction of arterial overwork.

10. Just as myocardial sufficiency is tested by counting the pulse, first in the erect and then in the recumbent posture, and noting that the less pronounced pulse retardation is in recumbency, the greater the degree of heart insufficiency, so may vasomotor sufficiency be determined. Normally, there is a postural variation in blood pressure. In the erect posture blood pressure rises owing to compensatory arteriole contraction, and this difference between recumbency and standing varies between 15 and 30 mm., according to my measurements with the Riva-Rocci instrument. In vasomotor insufficiency the postural variations are reversed, and this is especially true in neurasthenia, notably the angiopathic form. The bromides, carried to their physiological effects, will cause high blood pressure to fall, if dependent on augmented tonus of the vasomotor centre.

REVIEWS.

Obstetric and Gynecologic Nursing. By E. P. Davis, A.M., M.D. Philadelphia: W. B. Saunders & Co., 1904.

There can be doubt that less instruction is offered upon obstetrics to nurses in the course of their training than upon any other phase of their work. At least this is certainly true in this city, where several of the largest hospitals, those in which the best of training may be procured in general medical and surgical nursing, offer no practical instruction in this department of medicine. This being the case, there is room for a book upon this subject, particularly such a thoroughly good one as this.

The author's long experience in hospital work has placed him in a position to realize the needs of the nurse, and in his book he has carefully refrained from details of treatment and pathology useful alone to the physician, and has very clearly stated the duties of the nurse without, on the other hand, omitting anything of importance for her standpoint. His instructions, moreover, are most comprehensive and definite. For instance, in considering eclampsia he omits its etiology and pathology, contenting himself with detailing concisely the duties of the nurse while awaiting the arrival of medical help, and the same holds true in his discussion of post-partum hemorrhage. The chapter on "Obstetric Surgery" is excellent, and is illustrated in a manner which greatly enhances its value. The chapters upon the care of the newborn infant and the disorders which manifest themselves at this period of life are most satisfactory.

The last chapter in the obstetrical section is devoted to the development of the child, and in its ten pages it covers the ground well.

While most hospitals offer facilities for training pupil nurses in gynecological work there have been but few books published upon the subject for the use of nurses, and our experience has taught us that some such text-book as the present is urgently needed. The author explains the methods of the examination of gynecological cases, and gives among others most satisfactory chapters upon the use of douches, the preparation of the operating-room in private houses, the preparation and after-treatment of operative cases, and concludes with a most valuable appendix upon the preparation of surgical supplies.

We think that a most valuable and indeed the only addition to this portion of the work would be photographic reproductions of the various commonly used gynecological instruments.

W. R. N.

THE PRACTICAL MEDICINE SERIES OF YEAR BOOKS. OBSTETRICS. Edited by JOSEPH B. DE LEE, M.D. Chicago: The Year Book Publishers, 1904.

COMPOSED of a collection of edited abstracts of the best of the articles appearing within the current year, as are all the volumes of this series, there can be no question as to the important use subserved by them. A careful reading of the present volume, for example, will place one in possession of an epitome of the obstetrical advance of the past year which in itself would be ample justification for its publication. Moreover, as all references are, of course, given in full the volume serves as a very valuable index to current literature. Not the least valuable of the matter included is the section devoted to the subject of "Incubation," contributed by the author.

W. R. N.

PEDIATRICS. A Manual for Students and Practitioners. By HENRY ENOS TULEY, A.B., M.D., Professor of Obstetrics in the Medical Department of Kentucky University; Editor of Louisville Monthly Journal of Medicine and Surgery, etc. Illustrated by 33 engravings. Philadelphia and New York: Lea Brothers & Co., 1904.

THIS little volume of 258 pages is one of a series (the Medical Epitome Series) of condensed manuals of pocket-size which is now being published from time to time under the editorship of Dr. V. C. Pedersen, of New York.

The method of arrangement in a continuous text, following the classic text-book model, is a decided improvement over the usual question-and-answer form that has been so extensively used in brief treatises of this character, and thus dogmatic brevity and sacrifice of valuable space are advantageously avoided. The gain in dignity thus secured seems to be discounted to some degree in the volume before us by appending a series of questions at the end of each chapter, convenient as these may be for quizzing purposes. It is to be presumed, therefore, that popular demand has been consulted in retaining this essential feature of the quiz-compend. The subject has been very thoroughly covered from the birth of the infant to adolescence, including essentials of anatomy

and development, the care and hygiene of infancy and childhood, the examination of childish patients, the therapeutic peculiarities of young subjects, and the feeding of infants and older children. Following this the diseases of infancy and childhood are systematically discussed, with the necessary details of nursing and treatment. The style is brisk and pithy, well suited to the limitations of space demanded by the epitomic character of the work. The chapter on Infant Feeding, which is so important a feature of every work on the subject nowadays, is particularly full, covering thirty-three pages, or an eighth part of the whole; and the subject of home modification is discussed very completely. Altogether Dr. Tuley's work seems destined to take rank among the best, if indeed it is not the best, of those of similar scope now before the profession.

T. S. W.

A Manual of Clinical Diagnosis by Means of Microscopic and Chemical Methods for Students, Hospital Physicians, and Practitioners. By Charles E. Simon, M.D. Fifth edition, thoroughly revised and enlarged, illustrated with 150 engravings and 22 plates in colors. Philadelphia and New York: Lea Brothers & Co., 1904.

A book so well known as this one scarcely needs an introduction or detailed review. While the descriptions are concise and accurate, the scope of the book is very comprehensive, including chapters devoted to directions for the examinations of blood, secretions of the mouth, gastric contents, feces, urine, sputum, etc. The present edition has been much enlarged and thoroughly revised. Particularly noteworthy is the chapter upon the blood. Here we find accounts of the latest modifications and newer varieties of hæmatological instruments, as well as valuable and full descriptions of the new methods which have recently come into use for the staining of blood films. Advantage has been taken of the latest researches upon the histogenesis of the leukocytes in devising a classification of these cells. Although there is no encroachment upon the province of the larger text-books of hæmatology, some insight is given into conditions of the blood in various pathological states. The colored plates seem particularly successful. New material has been added to the discussions upon the bacteriology and parasitology of the blood, and, in fact, throughout the book one finds evidences of revision and enlargement. In the section dealing with transudates and exudates the subject of cytodiagnosis receives due attention. In all, the book forms an excellent guide for either practitioner or student, and will be of great practical assistance in the study of clinical diagnosis.

W. T. L.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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The Chemistry of the Urine in Diseases of the Pancreas.—CAMMIDGE (*Lancet*, March 19, 1904, p. 782) during the last three years has been studying the urine of patients with pancreatic disease in order to determine whether it be possible to recognize lesions of the gland during life as well as to differentiate the character of the lesion. In this investigation he was associated with Mr. Mayo Robson, whose extensive experience in surgery of the pancreatic gland is well known.

As a result of his study, Cammidge claims that it is possible to definitely determine the presence of pancreatic disease from the urinary examination. This is dependent upon the presence of glycerin in the urine, and the urinary test is practically that for glycerose. He asserts that fat necrosis is almost invariably associated with obvious disease of the pancreas. Although it is most typically met with in acute and gangrenous pancreatitis, he believes that it is not improbable that similar but evident changes accompany all forms of pancreatic inflammation. The local fat necroses are dependent upon the fermentative action of the pancreatic secretion. The fat of the tissues is converted into the fatty acids which enter into combination with lime, the other constituent of the fat molecule, glycerin, being absorbed into the circulation. This glycerin is eventually eliminated in the urine, and becomes converted into glycerose when the urine is boiled with a mineral acid, such as hydrochloric acid.

Cammidge describes in detail two tests for glycerose which he terms reaction "A" and reaction "B." Both are modifications of the phenylhydrazine test for glucose. Reaction "A" is briefly as follows: Ten c.c. of filtered urine are poured into a flask; add 1 c.c. of hydrochloric acid; place a funnel in the neck of the flask to act as a condenser and boil gently on a sand-bath for ten minutes. Add 5 c.c. each of filtered urine and distilled water, and allow the whole to cool in running water. Neutralize the excess of acid by adding slowly 4 gm. of lead carbonate, and, after allowing to stand for a few minutes, filter through a moist

filter paper, and wash out the flask on to the filter with 5 c.c. of distilled water. To the clear filtrate add 2 gm. of powdered sodium acetate and 0.75 gm. of phenylhydrazine hydrochlorate, and boil for three or four minutes on the sand-bath. Allow the contents of the flask to cool for twenty-four hours after pouring into a test-tube, and if pancreatic disease be present an abundant flocculent, yellow deposit collects at the bottom of the test-tube, which, when examined microscopically, is found to consist of sheaves and rosettes of yellow crystals. Before carrying out the test sugar must be examined for, and, if present, must be carefully removed by fermentation.

This reaction was not found entirely reliable, because the urine of patients suffering from certain diseases accompanied by active tissue changes, such as cancer, adenitis, pneumonia, etc., sometimes gave a positive result. Eventually reaction "B" was found to differentiate the pancreatic cases. This differentiating test depends upon the fact that the formation of the crystals described in reaction "A" is interfered with in inflammation of the pancreas by a preliminary treatment of the urine with perchloride of mercury, while such treatment does not affect the appearance of the crystals in cases of cancer of the pancreas and the other conditions which give rise to a positive reaction. By a combination of these two reactions Cammidge believes that it is possible to make a trustworthy diagnosis of pancreatic disease in most cases from the urine alone.

In reaction "B," 20 c.c. of filtered urine are thoroughly mixed with half its bulk of a saturated solution of perchloride of mercury. Allow to stand for a few minutes, filter, and to 10 c.c. of the filtrate 1 c.c. of strong hydrochloric acid is added. Boil for ten minutes on a sand-bath, and subsequently dilute with 5 c.c. of the filtrate from the mixed urine and perchloride of mercury and 10 c.c. of distilled water. Allow to cool, neutralize with 4 gm. of lead carbonate, and proceed from this point as in reaction "A."

The next step was to devise some means of differentiating the various forms of pancreatic disease, particularly chronic inflammation and cancer. It was at first thought that the mere size of the crystals would aid in differentiating the various pancreatic lesions. The crystals in malignant disease were, as a rule, coarser and broader than those in simple inflammation. Further, in simple inflammation the crystals from acute cases were, on the whole, somewhat finer than those seen in most instances of chronic inflammation. It was subsequently found that the solubility of the crystals proved more reliable than their size. If the crystals in reaction "A" be observed under the microscope while a 1:3 dilution of strong sulphuric acid is being irrigated under the cover-slip they will be seen to turn brown when the acid reaches them, and then to dissolve. Experience showed that the solubility of the crystals varied according to the length of duration and nature of the pancreatic disease.

Cammidge summarizes the practical results of urinary examinations in pancreatic disease by methods as follows: 1. If no crystals are found by either the "A" or the "B" method the pancreas is not at fault, and some other explanation of the symptoms must be sought. 2. If crystals are obtained by the "A" method but not by the "B" reaction active inflammation of the pancreas is present, and surgical interference is indicated. (*a*) The crystals obtained by the "A"

fractures by primary bone suture has for some time been the subject of discussion, but in Germany, at least, this method of treatment for fractures of the shaft of the humerus has been abandoned, and its use reserved for those fractures which are in the region of the ankle-joint. In supracondyloid fractures of the humerus, the Bardenheuer apparatus suitable for a fractured tibia is the one usually employed; however, in exceptional cases, where the fragments are widely separated it is best to use extension by weights, the forearm being placed in supination. The author notes five cases in which this method of treatment was most successful, while in another case the result was not so good. Passive motion of the elbow should be begun on the twelfth day, and this should be followed by careful massage of all the arm after the removal of the apparatus.

The Treatment of Gallstones Found as a Coincidence in Abdominal or Pelvic Operations.—CLARK (*American Medicine*, 1904, No. 2), after an admirable review of this most important subject, states, in conclusion: 1. The usual statement that 95 per cent. of gallstones produce no symptoms is fallacious, because it is drawn from autopsy and dissecting-room statistics. 2. Recent research points very strongly to the bacteriological origin of gallstones. 3. Bile is not bactericidal, for in the majority of cases of cholelithiasis micro-organisms of a more or less pathogenic nature are discovered. 4. Under these circumstances many more or less vague symptoms attributed to gastrointestinal or general constitutional disturbances may arise from toxins elaborated around these foreign bodies in the gall-bladder. 5. All clinicians admit that there is a wide hiatus in the clinical symptoms between the early formation of gallstones and the so-called classic attacks of biliary colic with jaundice. 6. Abdominal surgeons should make a most careful record of all gastrointestinal or hepatic symptoms and other vague epigastric pains, and associate these with an examination of the gall-bladder, with a view to establishing a further link in the symptomatology of cholelithiasis. 7. As cholelithotomy in a large series of cases has been attended with less than 2 per cent. mortality, the coincident removal of gallstones with some other abdominal operation is not a hazardous undertaking. 8. In the author's series of cases more than 50 per cent. have shown symptoms which could be unquestionably or with great assurance attributed to the presence of gallstones. 9. This coincident operation should be dictated by the most careful surgical judgment, for if the patient is in a critical condition from a prolonged operation, or the primary operation has been a septic one, this extra operation may be attended by serious results.

On the Prophylactic Use of Morphine in Cases of Severe Cerebral Injury.—MACDOUGAL (*Lancet*, June 25, 1904) states that his attention was attracted to this subject by the paper by Barr in the *British Medical Journal*, November 18, 1899, on "Meningitis," in which he calls attention to the excellent results that followed its employment in cases of this disease, and clearly showed that its beneficial action was due to the physiological effect upon the vascular and nervous systems inducing that condition of rest which, as Mr. Hilton has so admirably taught, is nature's opportunity. The author reports in detail three cases of very severe cerebral injury in which the sulphate of morphine in doses

of one-sixth of a grain hypodermically were administered from time to time, and the patients all made uninterrupted recoveries. All of the patients were subjected to operative interference as soon as they were seen. In all of the cases the use of the drug was continued for at least a fortnight at intervals of from six to eight hours, and its use would seem indicated in all cases of severe cerebral traumatism.

THERAPEUTICS.

UNDER THE CHARGE OF

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Electricity in Facial Neuralgia.—Dr. G. Dimier believes that the use of the continuous current is followed by the best of results in this condition. Certain observers advocate the use of a weak current—two to ten milliampères—while others prefer a current of from twenty to eighty milliampères; the author, however, considers the weaker current to be of sufficient strength. The negative electrode is placed at the back of the head, while the positive, which is of sufficient size to cover the distribution of the affected nerve, is placed upon the cheek. At each séance the current is applied from forty minutes to an hour. After the removal of the electrode the skin is red and congested, but this manifestation disappears within a few hours, leaving no trace, although desquamation may follow. After the séance the patient will experience relief and often a desire to sleep. Two or three treatments per week are sufficient in light cases, while daily applications are necessary in those of severity; it is also necessary that the treatments be at the same time of day, regularity and periodicity being essential. One should not be discouraged if no betterment is evident at the beginning, but the patient must be encouraged to persevere. At least three months are necessary to achieve a cure, the best method being daily or tri-weekly applications for this period, and eight or ten applications per month for several following months.—*La Quinzaine Therapeutique*, 1904, No. 7, p. 164.

The Treatment of Cutaneous Infections in Infants.—Dr. D'Astros discusses the local and constitutional treatment of these conditions as follows: The first indication is to sterilize the lesions so as to prevent further infection. This is best accomplished by means of a bath of 1:15,000 mercury bichloride, or an application of soap and water followed by naphtholated vaseline (1:10). Irritating applications are to be guarded against, lest they lessen the resisting power of the healthy skin and lead to a spread of the infection. Consequently the daily bath should be of simple boiled water, with the addition at times of a little sodium bicarbonate or boric acid. The dressings to be preferred are of simple sterile gauze. Zinc ointment combined with small quantities of boric or salicylic acid makes the best moist application,

while the most useful powder is a mixture of zinc oxide, talc, and bismuth subnitrate. Certain therapeutic applications, such as solutions of zinc or copper sulphate, are useful in impetigo, while in purulent conditions hydrogen peroxide is an acceptable antiseptic. Iodoform is powerful in this connection, but has disadvantages. Its use should be reserved for certain forms of ecthyma and cutaneous gangrene. In furunculosis, after proper washing with antiseptics and smearing of the surrounding parts with 10 per cent. boric acid in vaseline, the lesions should be incised, drained, and dressed with dry gauze. General treatment consists in proper feeding and hygiene, fresh country or sea air, tonics, and, in marked cachexia, subcutaneous injections of normal salt solution.—*Journal de Médecine de Paris*, 1904, No. 23, p. 232.

Euquinine in Malaria.—Large doses of this drug, according to Dr. K. B. Budberg, produce none of the unpleasant effects of quinine, and it is at least as powerful against malaria as the latter agent. On account of its lack of bitter taste it is easily administered to children, and its solubility in alcohol is an additional recommendation. It is an important fact that euquinine in sufficiently large doses (not less than 15 grains), and given about six hours before, will prevent an expected paroxysm. Smaller doses may have a like effect or only lessen the intensity of the paroxysm, or cause it to appear at irregular intervals. A single dose of from 15 to 20 grains often will, in recent cases, prevent further chills, but in chronic cases a recurrence is likely to take place within a week or two.—*St. Petersburger medicinische Wochenschrift*, 1904, No. 6, p. 53.

The Treatment of Itching.—M. F. Trémolierès considers the ideal treatment to be that which strikes at causes and regulates the polyuria, the oliguria, the hypoazaturia, the albuminuria, the cholæmia, the intestinal insufficiency, or whatever produces the pruritis. Various drugs taken internally may influence this distressing symptom—the author considers carbolic acid, gelsemium (which he believes dangerous), valerian, atropine sulphate, or valerianate (by mouth), arsenious acid, hydrocyanic acid, asafœtida, etc. In the pruritus of digestive origin and in senile and vulvar pruritus he recommends lactic acid, 6 to 10 drops of a 1 per cent. solution for infants; 15 to 30 drops for adults. External applications may be in the form of lotions, powders, or pomades. The following comprehensive formula is suggested: hydrocyanic acid, ½ to 1 part; mercury bichloride, ½ to 1 part; copper sulphate, 1 to 5 parts; carbolic acid, 5 to 10 parts; resorcin, 5 to 20 parts; chloral, 5 to 25 parts; potassium bromide, 5 to 50 parts; water, 1000 parts. Lotions of menthol and ichthyol, powders of bismuth, zinc oxide, salol, and salicylic acid are mentioned, as well as ointments of potassium cyanide, morphine, cocaine, belladonna, and calomel. Pruritus of the anal and genital regions may be treated by suppositories, lotions, and douches of very hot water, either pure or medicated. Above all, the local lesions, such as fissures, parasites, irritating discharges, etc., should be corrected. Moist dressings of 5 to 10 per cent. silver nitrate solution are useful here. Various physical means, the chief of which are hydrotherapy, electrotherapy, cutaneous occlusion, and climatotherapy are proper adjuvants in treatment.—*La presse médicale*, 1904, No. 51, p. 401.

PEDIATRICS.

UNDER THE CHARGE OF

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Status Lymphaticus, with Report of Cases. — R. A. BIECHELE (*Archives of Pediatrics*, July, 1904) carefully reviews the morbid anatomy of status lymphaticus, and reports several interesting cases.

The first case, although unconfirmed by post-mortem examination, is by reason of its history and course classed as status lymphaticus. The child, eleven months old, had been observed for the first time when six months of age. At that time she had enterocolitis, with thymic asthma and several slight convulsive seizures. Percussion revealed a marked increase of dulness in the region of the thymus; the tonsils were large, adenoids prominent, and there was some enlargement of the superficial lymph nodes. She recovered from the enterocolitis and remained well until the final attack. Following a slight fall convulsions supervened and continued for several hours. Then thymic asthma developed, which was followed by a short period of coma, and again convulsions, which continued until death occurred, twenty-four hours after the receipt of an injury so slight that under ordinary circumstances it would have passed unnoticed.

The relation of status lymphaticus to infection is illustrated by the following case: This child, twenty-two months of age, had always been in good health until the present illness. There had been a house epidemic of influenza, and this patient contracted the disease, which was typical, but apparently of mild character. Upon the second day, without premonitory symptoms, he developed convulsions, epileptiform in character, occurring at first at intervals of about thirty minutes. But in about two hours the convulsive explosions recurred with such rapidity as to be almost constant, and continued until death, about four hours after the first seizures and twenty-five hours from the time of the first evidence of infection.

The autopsy showed body well developed and nourished, with rickety manifestations. Upon opening the thorax a very large thymus presented itself, reaching from above the episternal notch well down over the pericardium and having two large lateral lobes. The organ weighed fifty-two grams, but the trachea was not compressed to any great degree. The heart and lungs were normal. The bronchial lymph nodes were enlarged. The spleen was enlarged, but of normal consistence. The agminated glands of the ileum were very large and elevated. The solitary follicles throughout the large intestine were very conspicuous. The mesenteric lymph nodes were exceedingly numerous, and upon section were succulent and of a translucent gray color. The

stomach was all but completely destroyed by self-digestion. Kidney and pancreas were normal, and the liver was of normal size and gray upon section.

Upon microscopic examination the thymus showed hyperplasia of the lymphoid elements. Hassal's corpuscles, which were numerous, showed a degeneration. There was a general hyperplasia of the lymphoid elements of the intestine.

The Albumin Content of Whey.—C. B. GRULEE (*Archives of Pediatrics*, June, 1904) gives the results of his experiments in determining the albumin content of whey.

The proteid percentage of whey, as given by various writers, ranges from 0.86 per cent. (König) to 1.02 per cent. (White and Ladd).

The writer obtained the following results: The average of a number of examinations was 0.5013 per cent., the highest 0.6616, and the lowest 0.2928 per cent. The work was conducted in the Laboratory of Physiological Chemistry of Northwestern University Medical School, and the following method was used: skimmed milk of pure quality and known to be stable in regard to the percentage of its constituents, was taken and raised to a temperature of 106° F., and rennet added in the proportion of one grain to the quart. After thirty minutes the curd was broken and removed by filtering through a wire sieve. The whey was heated to 150° F. to destroy the enzyme.

The whey was again filtered through Swedish filter paper, the sediment being small in amount. To 25 c.c. of this filtrate was added 1 c.c. of 25 per cent. acetic acid and three or four drops of 10 per cent. ammonium hydroxide and distilled water to make 100 c.c. This was boiled thoroughly and set aside until the coagulated albumin had settled.

The clear fluid was decanted through a Gooch crucible and distilled water added to the albumin left in the beaker. The supernatant fluid was treated in this manner several times, and the albumin was finally washed three times and then dried at 105° C. for two hours, at the end of which time it was cooled and weighed.

The drying and weighing were repeated until no difference in weight was obtained.

The writer believes that the various results obtained by experimenters in this line have been due to: 1. The milk. 2. The method of preparation of the whey. 3. The method of determination of the amount of albumin.

It is probable that most experimenters have prepared the whey by the use of liquid rennet and have determined the amount of albumin by the Kjeldahl process.

The writer used powdered rennet and the gravimetric process as described.

This method evidently procures a more perfect curding of the casein and leaves for the infant the more easily digested proteids.

Pollakiuria and Enuresis of Hysterical Origin in Children.—O. REINACH (*Jahrbuch für Kinderheilkunde*, 1903, Bd. viii., S. 795) reports two observations in children. The first patient was a girl, aged two years, intelligent and well developed, whose mother showed all the stigmata of hysteria, and whose father was neurasthenic. Following a terrifying dream, the child developed pollakiuria, voiding urine twenty

to thirty times in the twenty-four hours, and as frequently by day as by night. Sometimes she wet the bed, though she usually waked and cried vociferously. After this condition lasted two months the author conceived the idea of submitting her to painful faradization. This means of suggestion succeeded at once and prompt cure resulted. The same procedure was successful in the second patient, a girl, aged ten years, whose mother was manifestly hysterical.

GYNECOLOGY.

UNDER THE CHARGE OF

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OF NEW YORK.

ASSISTED BY

WILLIAM E. STUDDIFORD, M.D.

Castration after Hysterectomy.—BLUHM (*Zentralblatt für Gynäkologie*, 1904, No. 28) reports the case of a virgin, aged forty years, whose uterus was removed for malignant disease, the ovaries and tubes being spared. After the lapse of nearly two years she began to have such severe menstrual molimina that it was necessary to extirpate the ovaries. The writer thinks that this phenomenon is more apt to follow hysterectomies for cancer than for fibroid, hence he strongly advises the removal of the adnexa in the former cases, aside from the risk of metastasis.

Alexander's Operation.—STEIDL (*Zentralblatt für Gynäkologie*, 1904, No. 28) reports 60 cases extending over a period of two and one-half years; 38 for simple retrodisplacement, and 22 for retroflexion with prolapsus. He makes a crescentic incision above the pubes and does not open the canal. Non-absorbable sutures are used, and the wound is always drained. The patient is allowed to leave the hospital at the end of two weeks(!). Suppuration occurred in 12 cases. Of 49 patients who were examined at intervals of from two months to two and one-half years after operation all but 2 were permanently cured.

Primary Carcinoma of the Clitoris.—JACOBY (*Zentralblatt für Gynäkologie*, 1904, No. 30) reports two cases in which he operated, both having a recurrence in the inguinal glands. He collected reports of sixty-five other cases. The writer advises that every case of obstinate pruritus or eczema of this region should be regarded with suspicion as a possible forerunner of malignant disease, and in the event of enlargement of the organ a piece should be removed for microscopic examination. The only operation is extensive excision with thorough cauterization.

Results of Operation for Retroflexion and Prolapsus—BAATZ (*Zentralblatt für Gynäkologie*, 1904, No. 30) reports 217 operations for pro-

lapsus extending over a period of five years. His conclusions are as follows: All cases of prolapse of the vagina without retroversion should be treated by extensive plastic operations. In cases in which there is accompanying retroversion and prolapsus, with or without fixation of the uterus, ventrofixation should also be done. Vaginofixation with plastic operations is indicated in patients who have passed the climacteric, and rarely in cases of complete procidentia. In short, the writer prefers ventrofixation to shortening of the round ligaments as the routine treatment of retroflexion, whether the uterus is adherent or mobile.

Origin of Broad Ligament Cysts. — HANDLEY (*Journ. Obst. and Gyn. of British Empire*, 1903, No. 11) advances the ingenious theory that all cysts of the broad ligaments situated above the tubes, and which can be enucleated, develop through the distention of accessory tubes. This he infers because he has found such cysts communicating with normal Fallopian tubes, and showing on their inner walls folds identical with those found in specimens of hydrosalpinx.

Isolation of the Pelvic Cavity with a Flap of Peritoneum and Fascia. —KRÖNIG (*Zentralblatt für Gynäkologie*, 1904, No. 31) recommends this method of shutting off the pelvic from the general peritoneal cavity, especially after abdominal hysterectomy for cancer of the uterus. Instead of using peritoneal flaps alone, he strips off the parietal fascia also, both anteriorly and posteriorly. Two cases are reported, one of which terminated fatally.

Cause of Hemorrhage in Fibroids.—THEILHABER and HOLLINGER (*Archiv für Gynäkologie*, Band lxxi., Heft 2) from an examination of nineteen fibroid uteri demonstrated the erroneous nature of the view that the bleeding in these cases is due to hyperplasia of the endometrium. Atrophy of the mucosa was more often present than hypertrophy. The writers believe that the "myofibrosis" of the uterine wall is the true cause. In consequence of this condition the vessels cannot contract normally during menstruation. Muscular contractions in the tumor and excessive congestion from psychical influences are other factors.

Anatomy of Placental Polypi. — CURTIS and OUI contribute an extended article on this subject to the *Annales de Gynécologie et d'Obstétrique*, July, 1904, of which the following is a summary: The structure of placental polypus, or so-called *deciduoma benignum*, is more complex than is usually supposed. It includes both the fetal and the maternal elements of the placenta, has a special vascular supply, and is capable of continuous growth, like a true neoplasm. Its nutrition depends on variations in the maternal circulation, the imperfectly obliterated intervillous spaces being in direct communication with the vessels in the submucosa. The layer of Langhans and the syncytium tend to proliferate, but there is never any tendency to invasion of the uterine tissue, as Michaelis claims. The writers disagree with Hartmann and Toupet, who claim that the distinguishing feature of these polypi is the presence of bloodvessels in the chorionic villi. They regard the persistence of the syncytium as the principal element in the

diagnosis, since the latter cannot exist without a free vascular supply. The most important inference is that such polypi under unknown conditions may become malignant.

DERMATOLOGY.

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Papilloma of the Sole.—T. D. BERRY (*Journal of Cutaneous Diseases*, May, 1904) reports a personal case of this disease and refers to the case described by D. W. Montgomery in the *Journal of the American Medical Association*, July 11, 1903. The author, while designating the disease "papilloma," throughout his remarks refers to it as a wart. It was extremely rebellious to all manner of treatment, being finally cured by the Paquelin cautery, burning entirely through the skin of the sole and into the fatty cushion beneath, and then turning the point round and round until there was a hole left in which the blunt end of a lead-pencil could have been inserted. Six months later there was no recurrence.

Effect of Becquerel Rays upon Tissues.—HALKIN (*Arch. für Derm. und Syph.*, 1903, lxv. p. 201) found that the bloodvessels seem to be first affected, but that the action on these structures cannot be regarded as the cause of the other phenomena, much less that of the inflammation. There appears to be a lack of resistance of the bloodvessels due to a form of paralysis. In normal and in lupus tissues, after prolonged exposure daily for nineteen days, cellular degeneration, dilatation of the vessels, and hemorrhage was noted in the superficial layers, but the deeper layers were not affected.

A Series of Cases Treated by Radium.—HARTIGAN (*British Journal of Dermatology*, March, 1904, p. 105) brought before the Dermatological Society of Great Britain and Ireland a number of cases of cutaneous disease, chiefly rodent ulcer and lupus. The radium used weighed ten milligrams, and was contained in an excavation at the end of a vulcanite screw and covered with a mica plate, which in turn was secured by a brass cap having a window in it. It fitted into an outer vulcanite case, admitting of the screw being withdrawn or projected. The results obtained were very encouraging.

Reference may be made in particular to a case of nævus vasculosus or "port-wine mark" in a woman, aged twenty-six years, which had existed from birth, having since then extended somewhat. It was on the left cheek, extending from the eyelid to the upper lip and on the nose. The upper half received in all eight applications and the lower three

method will in acute inflammation dissolve in 33 per cent. sulphuric acid in about half a minute. (*b*) In chronic inflammation the crystals by the "A" method will take one or two minutes to disappear. 3. If crystals are found in preparations made by both the "A" and the "B" methods there may be (*a*) malignant disease of the pancreas, when the crystals will, as a rule, take from three to five minutes to dissolve, and operation is inadvisable; (*b*) a damaged pancreas due to past pancreatitis, when the crystals will dissolve in from one to two minutes; (*c*) some disease not connected with the pancreas, when the crystals will dissolve in about one minute. In the two latter, (*b*) and (*c*), the urgency of the symptoms and the condition of the patient must decide the need for an exploratory incision.

The writer believes that these methods are also going to be of service in differentiating pancreatic from non-pancreatic diabetes. This belief is based on practical experience with the test in one case of diabetes, which was subsequently shown at autopsy to be pancreatic in origin.

SURGERY.

UNDER THE CHARGE OF

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Osteoplastic Resection of the Symphysis.—MANZ (*Centralblatt für Chir.*, 1904, No. 15) states that the technique briefly consists in a skin incision which should be prolonged from either tubercle of the pubes downward. This incision should be continued downward until the angle of the pubic arch is reached, and all the parts should be freely dissected loose. Then by means of a wire saw the bone should be severed, the direction of the saw being in the direction of the obturator foramen; then taking a periosteal elevator the periosteum should be freely separated, the subsequent cutting of the bone being subperiosteal. By this means the contents of the lower pelvis are most accessible, and extirpation of the prostate or the urethra or the genital organs in women may be done with the greatest ease. When the operation is completed four wire sutures are amply sufficient to approximate the symphysis; then the incision of the skin should be closed in the usual manner.

A New Experiment in the Operative Treatment of Chronic Bright's Disease.—BAKES (*Centralblatt für Chir.*, 1904, No. 14) states that he has had such good results in one case treated by Edebohls' method that it demands to be published: The patient, a man, aged twenty-five years, had been under treatment for ten years in various hospitals

for a chronic nephritis of obscure etiology. Upon his admission to the hospital it was found that his case was typical of this disease, with marked œdema of the legs, ascites, etc. An examination of the urine showed it to be markedly albuminous and full of casts. Operation being decided upon, a bilateral decortication was performed, and the patient made an uninterrupted recovery, eight months later being sufficiently well to return to his usual occupation.

From the experience of this case it would seem that the weak point in Edebohls' method consists in a return of the denuded kidney back into its flat capsule, which of necessity contains but little tissue, and for that reason Bakes in completing the operation merely returned the kidney after removal of as much of this capsule as was possible, and he advises that instead of returning the kidney inside of its capsule, the kidney should either be enclosed in the mesentery or should be dislocated so that it is intraperitoneal when the raw surfaces are brought into intimate contact with the peritoneum. In regard to these two methods of disposing of the kidney, it would seem that it must depend not only upon the size of the kidney, but also upon the condition of the mesentery; and in those cases where the mesentery is found to be atrophied the intraperitoneal method would seem to be the best. In a subsequent operation a decorticized large white kidney was returned and placed between the mesentery, and the patient made an uninterrupted recovery.

Free Serous Exudation of the Peritoneum as an Early Symptom of Perforated Peritonitis.—HAEGLER (*Centralblatt für Chir.*, 1904, No. 10) states that as the result of animal experimentation he has learned that the quantity of the exudate stands in direct proportion to the amount or virulence of the germ material or its toxin that has been introduced. Under the author's direction, Thommen made a series of experiments on animals. Ten c.cm. of normal salt solution was injected intraperitoneally and the animals killed after various periods of time. These experiments showed that within the first six hours the amount of the intraperitoneal fluid was four times greater than the amount that had been injected; it consisted of an opalescent fluid very rich in albumin and which on standing became gelatinous. Intraperitoneal injection into a rabbit of 100 grams of distilled sterile water was followed in a few hours by an increase of from 30 to 40 c.cm. of this same albuminous fluid. The peritoneum reacts to all irritation very rapidly, and this reaction is shown by the excretion of a serous exudate, and it may be stated that absorption occurs in an almost similar length of time. This exudation into the peritoneal cavity is a movement of defence, as it were, on the part of the peritoneum to irritation or infection. In those cases of local inflammation of the intestinal wall the presence of free fluid in the peritoneal cavity should be considered as being unfavorable in weighing up the prognosis of the case. It shows that there is no tendency toward a restriction of the area of inflammation, for as soon as an attempt is made to restrict this inflammation adhesions very rapidly develop.

The Treatment of Supracondyloid Fractures of the Humerus by the Use of the Bardenheuer Extension Apparatus.—GRÄSSNER (*Centralblatt für Chirurgie*, 1903, No. 44) states that the treatment of all

applications, each of ten minutes' duration, and invariably after two or three applications a smart reaction followed, with vesication and the subsequent formation of scars, which later appeared as distinct, white areas.

Treatment of Lupus and Cancer by Light and Roentgen Rays.—R. B. WILD (*Medical Chronicle*, December, 1903) found that the Lortet-Genoud lamp was not so effective as the Finsen lamp or the Roentgen rays. For ulcerated surfaces and large areas the Roentgen rays were more useful than the lamp. Excessive reaction is cautioned against, the best results having been obtained when the reaction did not occur or was slight. In carcinoma the results were not satisfactory. Out of ten inoperable cases there was a fatal termination in nine, although in these cases pain was relieved and the discharge lessened.

Granuloma Fungoides Successfully Treated with X-rays.—LUSTGARTEN (*Journal of Cutaneous Diseases*, April, 1904, p. 185) records a case in which treatment succeeded after a long treatment of arsenic hypodermically administered had failed. The itching was a very notable and distressing symptom, which practically ceased after the first exposure. The lesions were fungoid and were widely distributed. A mild degree of inflammation of the skin developed under repeated exposures, but disappeared within a week, with a shedding of the epidermis. The patient was singularly susceptible to the rays, for a single twenty-minute exposure would produce an inflammation of the skin on any part of the general surface, followed by a complete disappearance of the lesion.

ELLIOTT (*ibid.*) has also observed excellent results from the same treatment in this disease, a case being referred to in which seventy-two exposures caused complete disappearance of all the lesions. Not all cases, however, are improved by this method of treatment, according to the experience of Dr. Duhring in a certain case.

The Staphylococci of Chronic Eczema.—F. VEIEL (*Münchener med. Wochenschrift*, January 6, 1904) examined cases of eczema madidans, moist and crusted, and found that in all forms and in all stages these organisms were present—generally yellow, sometimes white, and occasionally lemon colored. With few exceptions they existed in pure cultures. Tests were made to distinguish the saprophytic from the pyogenic forms, with the result that in every case the staphylococci of eczema seemed to be the same as the pyogenic forms, and the question is put forth, What part do they play in the production of eczema? It does not appear that anyone has been able by inoculation to have produced a chronic eczema, but it is highly probable that they must be regarded as influencing the disease and its course.

Creeping Eruptions.—L. P. HAMBURGER (*Journal of Cutaneous Diseases*, May, 1904) considers the whole subject at length. It has a special dermatological importance, and is worthy of note from a general medical standpoint because of its relation to myiasis, especially as applies to the bot-fly. The buttock is often the seat of the disease, pointing to the toilet as the possible seat of contagion. The feces may also be the carrier of the larvæ. The author describes a case occurring

in an imbecile boy, the lesion in the skin consisting of a serpiginous, curling, purplish, brownish, slightly crusted line situated on the right buttock, which gradually spread until an area the size of a hand was included. Excision of a piece of skin failed to discover a suspected parasite, but following the excision the line faded and the process ceased. Reference is made to the literature. The disease occurs more frequently in Russia than elsewhere, due to the bot-fly larvæ, but the parasite often escapes detection in a search for it.

Hyperidrosis Treated by Roentgen Rays.—ENGMAN (*Interstate Medical Journal*, 1903, x., p. 377) treated a case of this disease affecting the axillæ for three months until a dry erythema was produced, with loss of hair, with the result that there was improvement amounting to 50 to 75 per cent. Stelwagon (*Journal of Cutaneous Diseases*, 1903, xxi.) also found the same agent useful in sweating of the palms.

A Case of Bullous Lichen Planus.—M. F. ENGMAN (*Journal of Cutaneous Diseases*, May, 1904) reports a case, and concludes that the bleb formation is not a part of the pathological process, but that it may form in certain cases upon additional injury to the tissues through friction or accidental violence. It is a rare occurrence. The designation lichen planus pemphigoides would seem an appropriate name for the manifestation. A good photograph accompanies the article.

Dermatitis Exfoliativa Neonatorum, or Ritter's Disease—A. G. PATEK (*Journal of Cutaneous Diseases*, June, 1904) gives a case of this disease (rare in this country, although Ritter, in Germany, in ten years observed nearly 300 cases), and states that it is liable to be confounded with pemphigus foliaceus, acute pemphigus, and syphilis. The clinical history points to a septic nature, which view is corroborated by Ritter's experience, that it occurred in epidemics in foundling asylums. It is infectious, though Ritter has much evidence to show that contagion plays no part in its spread.

Patek found diplococci in the serum of lesions, but states that a diplococcus has been found also in pemphigus, observers remarking upon its resemblance to the gonococcus. Most observers have, however, isolated a micrococcus that in two cases gave rise, upon inoculation, to typical pemphigoid bullæ. It is probable, the author thinks, that there is confusion in the diagnosis of the two diseases, although it is possible to make a correct diagnosis.

Dermatitis Herpetiformis in Children.—MEYNET and PEHU (*Annales de Derm. et de Syph.*, December, 1903) conclude that the disease occurs more often in the later than in the earlier period of childhood, from six to ten years being the commonest period; that males are more affected than females (17 to 7); that no single cause can be stated to exist in the majority of cases, and that there is no reason for making a distinct group of children's cases as proposed by Unna.

Acute Infectious Pemphigus in a Butcher.—J. T. BOWEN (*Journal of Cutaneous Diseases*, June, 1904) finds this case interesting, because it occurred at a period when epizoötic foot-and-mouth disease prevailed in New England, a year ago. The eruption of blebs was evi-

dently due to an infection from a wound in a man engaged in butchering. Reference is made to the reports of like cases by Pernet and others. The evidence is not sufficient to prove that the virus of foot-and-mouth disease (usually mild both in animals and man) was a factor in this case. In acute pemphigus no other agent than an inoculated infection seems tenable, the process being a febrile infectious disease running an acute course.

Histological Investigation of Some Well-known Reducing Drugs in Skin Diseases.—VIGNOLO LUTATI (*Monatshefte f. Prakt. Derm.*, March 15, 1904) experimented on a cock's comb with tar, anthrarobin, gallacetophenon, and ichthyol. The action of tar is not merely superficial, but extends deep into the corium. Oleum rusci is more stimulating than oleum cadinum. Anthrarobin acts similarly to chrysarobin, and the author thinks that it might well replace the latter in practice.

Gallacetophenone is less stimulating than pyrogallol, more so than anthrarobin, and more like chrysarobin. The changes observed under the microscope are given in full.

Treatment of Various Forms of Cutaneous Disease by X-rays and Light.—W. A. JAMIESON (*Scot. Med. and Surg. Journ.*, February, 1904) refers to 133 cases of lupus vulgaris treated by himself during eighteen months, a large proportion being treated by the *x*-ray, others by the London Hospital modification of the Lortet-Genoud lamp. The latter method is regarded as superior in lupus to the *x*-ray in that it did not produce burns, although less useful, owing to its restricted employment and slowness of action, and consequently he has abandoned it, inasmuch as the beneficial effect was not commensurate with the expense. The results in rodent ulcer with the *x*-rays were good, and he advises, first, the removal of the growth by scraping, followed by chromic acid fused on the point of a probe applied to restricted areas at a time. Excellent results were obtained in mycosis fungoides.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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Bacilli in the Air Exhaled by Consumptives.—It has been accepted very generally that the air exhaled by consumptives during quiet respiration contains no tubercle bacilli or other bacteria, but this has been shown by Dr. W. Koelzer (*Zeitschrift für Hygiene und Infectionskrankheiten*, xliv., p. 217) to be not wholly true. This general belief is based upon the fact that even fairly strong currents of air are incapable of taking up bacteria, moulds or other matters from moist surfaces, unless at the same time the latter are subjected to some mechanical violence. Koelzer experimented with fifteen patients, who were allowed to breathe gently for from seven to fifteen minutes against sterile Petri dishes held two to three inches away from their mouths, proper pre-

cautions being taken to exclude all possible error from coughing, sneezing, speaking, and forced respiration. Of thirty guinea-pigs inoculated with the gelatine contents of the dishes, but one became infected; and this one died in ten weeks of typical general tuberculosis. It is especially significant that the dish the contents of which this animal received was one which was exposed to the patient who was the sickest of the group and the only one with laryngeal lesions. The liberation of the bacilli in this instance is attributed to the constant vibration of the vocal cords or to the bursting of minute bubbles, which occurs when the moist cords move apart from each other. It is suggested, however, that bacilli may be given off to the respired air by the bursting of bubbles (rales) in the fine bronchi, for the bursting of every bubble of mucus is accompanied by liberation of the finest particles of fluid, invisible to the naked eye, some of which may not fall back and become attached again to the surface of the tube, but may escape to the outer air. Naegeli and Buchner demonstrated more than twenty years ago that the bursting of fine bubbles caused by the ascent of air currents through a bed of sand impregnated with pure cultures of bacteria, projected bacteria four inches vertically. Since particles of coal-dust may reach the alveoli in inspiration, there can be no doubt that equally minute particles from the lungs may escape during expiration. Foelzer expressly disclaims any suggestion that his results are of any great practical importance, for the number of bacilli expelled in this way must be as nothing to those in suspension from dried and pulverized sputum and from sprayed droplets caused by coughing, sneezing, and speaking. His conclusions are summarized as follows: 1. The sentence "The air of quiet respiration of consumptives is free from tubercle bacilli" should be amended to read as follows: "The air of quiet respiration of consumptives is not germ-free, yet the exhalation of tubercle bacilli occurs only under peculiar conditions, and then to such a slight extent that, from a practical point of view, the expired air may not be considered as an essential source of infection." 2. The source of the infectivity of respired air is the spraying of mucopurulent material in the lungs, which we hear as rales. 3. The bacilli liberated in quiet expiration are so few in number that they can easily escape exact experimental demonstration. 4. The possibility of infection through quiet respiration is very remote in comparison with that offered by the pulverization of sputum and the spraying of sputum in coughing, sneezing, and speaking. 5. Severe laryngeal tuberculosis favors the infection of expired air quantitatively to such an extent that the bacilli can be exhaled in numbers sufficient for experimental demonstration.

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A STUDY OF ULCER OF THE STOMACH AND DUODENUM.

BASED UPON A SERIES OF EIGHTY-TWO CASES.

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(From the Clinic of Professor Osler.)

It is only by a careful study of a series of cases of any one disease that a general and comprehensive picture of the condition can be obtained. Moreover, an analysis of the cases of "round ulcer" at the Johns Hopkins Hospital is of particular interest, as the disease has here been regarded as comparatively rare.

Etiology. *Incidence.* In the analysis ulcer of the duodenum has been included, as physiologically, clinically, and pathologically the first part of the duodenum is identical with the stomach.

In all, 82 cases of round ulcer have occurred in the medical, surgical, and gynecological services from the opening of the hospital on May 5, 1889, to May 1, 1904—a period of about fifteen years. There has been a total number of 44,338 admissions to these services, which gives for the hospital a frequency of 0.18 per cent. According to service, the admissions are: 17,043 medical, with 76 cases; 16,553 surgical, with 4 cases; 10,961 gynecological, with 2 cases.

The surgical series includes only cases that were admitted primarily into that service, and is exclusive of the 11 that were transferred from the medical side for operation.

In this series there were six* duodenal ulcers—four in the medical and one each in the surgical and gynecological services.

* Since writing, the record of a subsequent admission of a supposed case has been found. The autopsy showed a ruptured œsophageal varix accompanying a cirrhosis of the liver to be the source of the hemorrhage. The local signs are difficult to explain, as no ulcer was found in the duodenum or stomach.

We have elsewhere* given comparative clinical data as to the frequency of ulcer (exclusive of duodenal) in some of the leading hospitals of Europe and America. We will recall some of the more striking figures: Edinburgh, 2.02 per cent.; Berlin, 1.33 per cent.; Boston, 1.28 per cent.; Montreal, 0.92 per cent.; London, 0.78 per cent.; New York, 0.44 per cent.; Baltimore, 0.37 per cent.; Denver, 0.12 per cent.

Hence we conclude that gastric ulcer is relatively rare in Baltimore.

Sex. The older writers state that ulcer of the stomach is more frequent in women, in the ratio of 2 to 1. Welch[1] found that in 1699 cases the ratio was 3 to 2. Mayo,[2] in the operating-room, found 59 per cent. in women and 41 per cent. in men. Greenough and Joslin[3] found in Boston a remarkably high ratio of females to males (5 to 1), "though no such disproportion exists in the total number of males and females admitted to the hospital." We could find only one higher ratio than the above, viz., 14 females to 1 male (quoted by Fiedler).

In our series there were 48 males to 28 females—a ratio of almost 2 to 1 in favor of the males. Now the ratio of total males to females for all services is 1 to 1, but 2 to 1 for the medical, from which the vast majority of our cases is taken. Hence it will be seen that gastric ulcer with us is *relatively* as common in men as in women, contrary to the usual idea.

Duodenal ulcer is more frequent in males. Osler[4] collected 178 males to 41 females—a ratio of more than 4 to 1. Mayo[2] found 20 males out of 24 cases at operation. In our series there were 5 males to 1 female—about the generally accepted proportion.

Age. Most authorities, notably Welch in his classical monograph in Pepper's *System*, give the most frequent period for both sexes as between twenty to forty years; for the males, twenty to thirty years, and females, thirty to forty years. Greenough and Joslin's figures tally with this. Calwell,[5] in an analysis of 193 cases, found that in the male only 3 cases occurred before twenty-five years, while in the female there were no cases before thirteen, but the majority were between the ages of fifteen and twenty-five.

According to our table the larger number of all cases (32.9 per cent.) occurred between the ages of forty to fifty. In the males 41.5 per cent. occurred between the ages of forty to fifty—a decade later than usual; while in the females 44.8 per cent. occurred, as usual, in the third decade.

As one might expect, there were none in the first decade, and only 3 in the second, all of whom were girls. This rarity in early life is well recognized. Welch found only one instance of the disease in the first decade of life among the 607 cases which he col-

* Medical News, 1904, vol. ii.

lected. At the Baby's Hospital of New York there were only 5 cases in 390 autopsies. Fenwick,[6] in 1900, was able to collect from the literature only 18 cases in children. There were in our series 20 patients over fifty years of age—many of them coming under the category of "senile ulcer"—a condition often difficult to differentiate from carcinoma.

TABLE I.—SHOWING PROPORTION OF SEX AND AGE IN GASTRIC AND DUODENAL CASES.

Decades.	Total cases.	Per cent. of total.	Total males.	Per cent. of males.	Total females.	Per cent. of females.
1 to 9	0	0	0	0	0	0
10 " 19	3	3.6	0	0	3	10.3
20 " 29	17 (1 d.)	20.7	4	7.6	13 (1 d.)	44.8
30 " 39	15 (1 d.)	18.4	11 (1 d.)	20.7	4	13.9
40 " 49	27 (2 d.)	32.9	22 (2 d.)	41.5	5	17.2
50 " 59	14 (1 d.)	17.1	12 (1 d.)	22.6	2	6.9
60 " 69	5	6.1	3	5.7	2	6.9
70 " 79	1 (1 d.	1.2	1	1.9	0	0
	82	100.0	53	100.0	29	100.0

CONJUGAL CONDITION plays no role in the male. Of the 29 women, 16 of them were nulliparæ, 5 primiparæ, and 8 multiparæ.

RACE. Of the 82 cases, 67 were white and 15 were colored—a ratio of 4.5 to 1. As regards admission, the ratio is 7 to 1. Therefore, among our cases ulcer is relatively more common in the colored race, which fact does away with a recent suggestion that the rarity of ulcer in Baltimore is due to the number of colored admissions. We could find no other figures on this point.

NATIONALITY. Fifty-eight of our series were born in various parts of the United States—16 in Germany, 3 in Russia, 2 each in Scotland and Ireland, and 1 in Switzerland. The relative proportion of American-born to German-born patients is 13.6 to 1, while in our series it is 3.6 to 1—*i. e.*, ulcer is relatively more frequent among the Germans. This bears out our figures on the relative incidence of ulcer in America, which show that on this continent the percentage is 0.57, as compared with 0.78 per cent. of London, and 1.33 per cent. of Berlin.

OCCUPATION. Much stress was formerly laid upon occupation as a predisposing cause. Greenough and Joslin could not find any one occupation especially prone to the disease; thus 66 per cent. of the females were housewives, while of 200 consecutive female admissions there were 71 per cent.; again, only 7 per cent. were cooks as compared with 4 per cent. of general admissions. In our series 12 of 29 females did housework (41 per cent.), and only 3 were cooks (10 per cent.). Of 53 males there were 9 laborers and 9 merchants—*i. e.*, 17 per cent. of the cases were divided equally between the upper and lower walks of life. Bramwell believes that

ulcer is more common in the hospital class than in well-to-do patients —a point to which Robson rightly takes exception. Again, there were only 2 tailors and 1 shoemaker—occupations considered especially prone to the disease. The only part that occupation can play is that the in-door pursuit, on account of its sedentary nature, is more predisposing to ulcer than the out-door. Thus, in our series the proportion is nearly 4 to 1 (61 in-door to 14 out-door).

Family History. Heredity plays little or no part. In 8 cases (9.7 per cent.) there was a history of stomach trouble other than cancer, but in none was there any special suggestion of ulcer. In another 8 cases there was a definite history of carcinoma twice of the stomach (2.4 per cent.). Statistics elsewhere are unsatisfactory, though Drechsfeld succeeded in eliciting a family history of ulcer in 8 cases.

Previous Stomach Trouble. In 47 of the series (57.3 per cent.) there was a definite history of this for some months prior to the onset of symptoms suggestive of ulcer, though in many it was difficult to draw the line between the two. In the majority it was described as "indigestion," as shown by discomfort after certain articles of food, eructations of gas and pyrosis.

Chlorosis has been considered an important factor, especially among young females. Exact figures on this matter are difficult to obtain, though Osler states that "anæmia and chlorosis predispose strongly to gastric ulcer, particularly in women and in association with menstrual disorders." In 72 per cent. of Fenwick's series there was a definite history of chlorosis (pallor, œdema, and dyspnœa) before the first symptoms of ulcer were manifest. In only 9 of our cases (11 per cent.) was there a definite history of chlorosis.

Trauma. There was a positive history in 7 (8.5 per cent.). In 4 it was "direct violence," as a blow or fracture of ribs; in 1 "strain," and in 2 merely "injury." Burns may cause ulceration, but usually of the duodenum; of the latter there has not been an example in about 2300 autopsies at the Johns Hopkins Hospital.

Alcohol. In a large proportion (53.6 per cent.) there was a history of the use of alcohol, and in 19.5 per cent. to excess. How far this predisposes to ulcer it is difficult to say. Lancereaux thinks ulcer is more common in drunkards, especially those who drink ardent spirits. The weight of opinion regarding the "bodily ills" that are due to alcohol is at present turning the other way.

Syphilis. Syphilitic ulcer of the stomach is rare, and differs materially in its appearance and symptomatology from simple ulcer. We are not concerned with it in this paper. Nevertheless, in our series there was a definite history of syphilis—either recent or old—in 15.8 per cent Fenwick found such in 10 per cent. of the chronic cases. The etiological role that syphilis may play consists probably in the production of a specific endarteritis.

Tuberculosis. In our series, which does not include specific tuberculous ulcers, tuberculosis in one or another of its manifes-

tations was present in 13.4 per cent. of the cases, as shown post-mortem, or clinically by the sputum. Fenwick found such in 17 per cent. of his series There is no evidence in the literature that tuberculosis predisposes to ulcer. In Brinton's opinion, however, ulcer of the stomach predisposes to tuberculosis. Welch[1] says: "The large share taken by pulmonary phthisis in deaths from all causes renders the disease a frequent associate of gastric ulcer. It is *probable* that the lowered vitality of phthisical patients increases somewhat the liability to gastric ulcer."

Diseases of the Heart and Bloodvessels. Arteriosclerosis may play some part, as it predisposes to thrombosis, which is undoubtedly of importance in the pathogenesis of round ulcer. It was present, as shown clinically by palpation of the peripheral vessels or post-mortem by macroscopic changes, in 48.8 per cent. of our series; to a marked degree in 22 per cent.

Endocarditis should also be considered, as it may give rise to embolism, which has been regarded by some as an important etiological event. Valvular disease of the heart was present, as shown by undoubted physical signs or at autopsy, in 8.5 per cent. No regard is taken of merely hæmic murmurs which were noted in 5 other cases.

Symptomatology. *Complaints.* These were various, but in 50 per cent. "pain" was the chief complaint. In another, 47.5 per cent., "stomach trouble;" "dyspepsia" or "vomiting" were the symptoms from which they sought relief. In only 5 cases (6 per cent.) was a history of "vomiting of blood" volunteered by the patient.

Mode of Onset. There were only 8 cases (9.7 per cent.) that might be termed *acute*, of which two developed in the hospital during the course of another disease; 2 developed twenty-four hours before admission; 3 three weeks, and 1 four weeks before admission. The remaining 74 were examples of *chronic* "ulcer" having existed for periods ranging from two months to twenty years.

The Three Cardinal Symptoms. The order of frequency of these will be seen in Table II., where they are contrasted with those given by Greenough and Joslin,[3] and those of Fenwick. For comparison's sake we have also added those of Osler and McCrae[7] in their analysis of the carcinoma cases in this institution.

Table II.—Frequency of Vomiting, Pain, etc., in Gastric Ulcer.

Symptoms.	Johns Hopkins Hospital. (82 cases.)	Greenough and Joslin. (187 cases.)	Fenwick (chronic). (265 cases.)	Cancer series (J. H. H.) (150 cases.)
Vomiting . . .	85.3 per ct.	95.7 per ct.	72 per ct.	85.3 per ct.
Pain	82.9 "	92 5 "	100 "	86.6 "
Hæmatemesis . .	75 6 "	78.6 "	71 "	28.1 "
	Exclusive of melæna.	Exclusive of melæna.	Inclusive of melæna.	Exclusive of melæna.

By this it will be seen that the order of frequency in ours is similar to that of the Boston writers, though all three symptoms are somewhat more frequent in the latter. On the other hand, Fenwick's figures from London for 265 chronic cases are somewhat different, pain being present in 100 per cent.; while vomiting and hæmatemesis are of practically equal frequency, they are considerably less common than in either of the preceding series. The cancer figures are interesting, pain and vomiting being present in the vast majority, while hæmatemesis, as one might expect, is three times less frequent than in ulcer in our series.

PAIN. This symptom is usually the first indication of the existence of an ulcer, and is the most constant and distinctive feature. But pain is only a relative matter, and is the most difficult of all data to estimate. It was present in 82.9 per cent. of our cases. It usually means an active ulcer or its sequelæ. Leube believes that cicatrices cause pain only in very rare instances.

Site. Pain is usually referred to the epigastrium, as was the case in 54.4 per cent. of our series. Occasionally it is referred to the spine or left shoulder-blade (14.7 per cent.); more rarely to either hypochondrium (8.8 per cent.). In 2 cases the sternum and right iliac fossa were the respective locations. That the situation of the pain may give a clue to the site of the ulcer was maintained by Brinton. This is not accepted by the more recent authors. Of the 27 cases in which the site of the ulcer was determined at autopsy or exploratory operation, the site of pain was entirely misleading in 3 cases, of no definite value in 17, while in another 7 it only pointed to the pylorus or the duodenum.

Character. The pain is usually severe, though it may not exceed that of hyperchlorhydria. It is rarely continuous (4.8 per cent.), but if so usually means some complication as perigastric adhesions, localized peritonitis, or hyperchlorhydria. The *quality* of the pain is variously described as "sharp" (20.3 per cent.), "dull aching" (18.6 per cent.), "burning" (15.2 per cent.), "colicky" (13.5 per cent.), "gnawing or grinding" (11.9 per cent.), and as "boring," "cutting," "tearing," etc., in the remaining 22.5 per cent.

Pressure usually increases the pain, but may afford relief. The statements of different observers on this point are at great variance. In 24 cases where inquiry was made with regard to the question, increase of pain was present in 62.5 per cent., relief in 33.3 per cent., and no relief in 4.2 per cent. Again, pain is influenced by *posture.* Thus, out of 10 cases in which note is made of this, relief was experienced in 6 either by lateral or dorsal decubitus, "knee-and-chest" or upright position. Osborne's contention that the site of the ulcer may be inferred from the effect of posture on the pain, could only be tested in 2 cases, and without satisfactory result. In 1 case, where the ulcer involved the entire circumference of the pylorus,

dorsal decubitus gave relief, while in a duodenal ulcer with stenosis either lateral posture was helpful.

The relation of pain to *ingestion of food* is important. It is usually increased by eating (39 per cent.), but may be relieved (14 per cent.), or, again, be entirely independent of food. Gerhardt maintains that patients who are afraid to eat because they *fear* pain are usually suffering from simple ulcer and not cancer. There was "no pain" in only 4 cases, though in another 10 no mention is made. Some have called attention to the fact that cases of ulcer of the stomach without pain represent a grave type of the disease. In our series of four, 3 died, 2 from hemorrhage and 1 from a complication. In Boston 3 of 14 cases without pain were fatal.

Vomiting is the commonest symptom in our series (85.3 per cent.). There is a close relation between the severity of the pain and the vomiting. In the majority (67.2 per cent.) it is frequent, occurring almost constantly in a few cases; in others periodically. It is usually involuntary, but in some it may be provoked for the relief it affords, as was the case in 3 of our series. Again, in a certain number of cases (20.7 per cent.) it is only "only occasional," following some particular paroxysm of pain or the ingestion of certain foods. In a small percentage (12) it is the exception, and not the rule. The *quantity* varies greatly, but is profuse only where there is either hypersecretion or pyloric obstruction. Emesis generally depends upon the *ingestion of food*, and occurs at the height of digestion or immediately after taking food into the stomach. This was the case in 14 out of 20 where this point was noted It usually affords relief (as was the case in 15 of our series) by removing the cause of irritation, viz., the food and acid-juice. In 7 cases there was an entire absence of vomiting. These merit a moment's consideration; 5 ran a moderate course, 1 being discharged well, and 4 improved; the other 2 were more severe, 1 dying in the hospital, and 1 four weeks after discharge. The autopsy on the former (Case 15), revealed a large eroding ulcer upon the lesser curvature and posterior wall near the pylorus, with erosion of the artery, perforation of the wall, and exposure of the pancreas beneath. This one case conflicts with the statement "that vomiting is never absent when an orifice of the stomach is involved."

Relation of Vomiting and Pain to the Site of the Ulcer. Of the 23 cases that came to autopsy or exploratory operation, the site of the ulcer is specified in 22. In ulcer of the pylorus vomiting was almost constant, as was also pain, although to a somewhat less extent. In involvement of the lesser curvature vomiting and pain were present in a third of the cases only. In 4 cases in which the posterior wall was also involved, vomiting was present in 3 and pain in all 4. In the 1 case, in which the anterior wall was also involved, both were present. In 4 cases with ulcer on the greater curvature involving either wall pain was present in three instances,

vomiting in all. In 1 of the 2 cases in which the lesion was on the posterior wall alone, both were present. Thus, vomiting was present in 17 out of 22 cases, more constantly where either orifice or the greater curvature was involved than when the ulcer was on the lesser curvature. Pain, on the other hand, was practically constant except in ulcer of the pylorus or lesser curvature.

TABLE III.—RELATION OF VOMITING AND PAIN TO SITE OF ULCER.

Site of ulcer.	No. of cases.	Vomiting.	Pain.
Pylorus	8	7	5
Lesser curvature	3	1	1
Lesser curvature and posterior wall	4	3	4
Lesser curvature and anterior wall	1	1	1
Greater curvature (near cardia)	1	1	1
Greater curvature and posterior wall	1	1	...
Greater curvature and anterior wall	2	2	2
Posterior wall	2	1	1
	22	17	15

HÆMATEMESIS. Vomiting of blood is usually not so constant a symptom. It was, however, present in 75.6 per cent. of our series, as compared with 78.6 per cent. of the Boston cases. The older writers give a much lower frequency. Thus, Brinton, 28 per cent.; Müller, 32 per cent., and Gerhardt, 47 per cent.

The *color* is noted in 56 cases; "coffee-ground" in 66 per cent.; bright red in 33 per cent. "Coffee-ground" vomiting occurs whenever the blood remains sufficiently long in the stomach to be acted upon by the gastric juice, and does not necessarily imply malignancy. On the other hand, "bright blood" was present in 11 per cent. of the cancer series in which hæmatemesis occurred. The *quantity* was usually fairly large; in 86.1 per cent. it was more, and in 18.9 per cent. it was less than two drachms. Severe hemorrhage may cause instant death without external evidence. This "l'hémorragie foudroyante" occurs, according to Brinton, in 5 per cent., and Fenwick in 3.4 per cent. There was one example of this in our series (Case 65), in which an aneurysm of the thoracic aorta being present, its rupture was thought to be the source of hemorrhage, until the autopsy revealed an ulcer eroding the gastric artery. The *number* of the hemorrhages is also variable. Thus there were—

One hemorrhage	7 cases.
Two hemorrhages	7 "
Three hemorrhages	11 "
Four hemorrhages	1 case.
Many hemorrhages	15 cases.

In about 40 per cent. of Fenwick's cases it recurred in a week, in 73 per cent. in twelve months after its apparent cessation. The factor which determines the recurrence, Moynihan[8] thinks, is the stretching of the ulcer from distention of the stomach. This latter condition he found in all of 15 ulcer cases in which he operated

for hemorrhage. Hæmatemesis sometimes gives almost immediate relief to the pain and vomiting. Of the 16 cases in which no hæmatemesis occurred ulcer was found in 5 at autopsy and 1 at operation; in the remaining 10 the diagnosis was supported by other data, such as melæna, local tenderness, vomiting, etc. As to the frequency of hæmatemesis at the menstrual period we have no data. In two of the Boston series the first hæmatemesis occurred at this time.

Melæna. Severe hemorrhage from an ulcer invariably gives rise to tarry stools, but, according to Hosslin, only when the blood amounts to 500 c.c. Melæna can occur without hæmatemesis in an ulcer near the pylorus or in the duodenum. In 55 cases in which there was a clear history as to its occurrence or non-occurrence melæna occurred in 80 per cent. The statements of patients are not reliable on this point, and often give one an altogether erroneous idea. There is no doubt that a careful, systematic, routine examination of the stools would reveal blood in the vast majority of cases.

The *color* was dark and tarry in 8 per cent., and bright red in 20 per cent. of 28 cases. The color varies, of course, according to the size, freshness, and rapidity of the hemorrhage and the length of time the blood takes to pass through the intestinal tract. The *quantity* was large in 9, small in 6. The *number* of times in which melæna was observed varied from a few in 17 to many in 10.

Of the 44 positive cases, 36 accompanied or followed the vomiting of blood; 8 gave no history of hæmatemesis; 1 of these was regarded as duodenal, and 5 were considered gastric ulcer; 2 were shown at autopsy to be gastric ulcer.

Nausea was present in 32 out of 34 cases. That this symptom was not noted in the remaining 50 cases suggests that it is relatively uncommon. This is natural, for the vomiting is a result of the pain and a desire on the part of the patient or his stomach to be rid of irritating material. A recent writer[9] says: "A feature to be remembered about the vomiting is that it is not usually accompanied by nausea, and does not require much effort."

Dyspepsia. By this term we include discomfort after eating, eructations, pyrosis, headache, palpitation, meteorism, etc. It was present in 96 per cent. of 52 cases. It is of little or no importance, and generally dependent upon the attendant hyperchlorhydria and chronic gastritis, both of which usually accompany the disease. Digestion, then, is not, as a rule, more difficult or restricted in uncomplicated cases.

Appetite. This may be lost (5.9 per cent.), variable (4.4 per cent.), poor (45.6 per cent.), or good (44.1 per cent.). Others have found that as a general rule the appetite is good. The dictum that in ulcer the appetite is good, but patients *fear* to eat, while in cancer the appetite is lost, is an important aid to diagnosis.

Bowels. Constipation is the rule, as was the case in 61.6 per cent. here and 80 per cent. in Boston. Greenough and Joslin ascribe their large percentage to the greater frequency of the disease in women. The latter was not the case in our series, which may account for the lower percentage in which constipation was present. The most important cause is the small amount of solid food taken and retained by the patient. In 10.9 per cent. there was "looseness" if not actual diarrhœa. In the remaining 27.5 per cent. the bowels were regular.

General Health. The usual teaching that moderate loss of weight and strength are present is not borne out. In none was cachexia noted, but in a very large number was there loss of strength (98 per cent. of 47 cases) and loss of weight (87 per cent. of 62 cases) noted. These are due partly to the pain and inability to eat, and partly to the loss of blood. I think the number of cases (87.1 per cent.) in which loss of weight occurred is of interest. The details are given in Table IV.

Loss of weight (no figures)	15		
Slight (1–5 lbs.)	1	10–20 lbs.	10
Moderate (5–10 lbs.)	2	20–30 lbs.	7
Marked (10 lbs. or more)	36	30–40 lbs.	10
		40 + lbs.	9
	54		36

Of the 9 that lost forty pounds or over, there were 3 that lost forty pounds; 2, forty to fifty pounds; 2, forty-six pounds; 1, fifty pounds, and 1, seventy-five pounds. Such a marked loss of weight would naturally suggest malignant disease, but it must be borne in mind that pain, coffee-ground vomitus, tumor, and marked loss in weight can all be present in benign ulcer of the stomach.

Physical Signs. *Tenderness* is the least important of the cardinal symptoms or signs. Its absence or presence is responsible for many errors in diagnosis. It was noted in 57.9 per cent. of our series as compared with 69.5 per cent. in Boston. The *degree* varied from one extreme to another; thus, 2 cases could not bear the pressure of the clothing, while in others considerable pressure was required to elicit any discomfort.

Site. It was usually localized to a small area in the epigastrium (75 per cent.), but in others it was general over the upper abdominal zone. It was present in the left hypochondrium (10 per cent.); in the right hypochondrium (5 per cent.); right iliac fossa (5 per cent.), and in umbilical zone (5 per cent.). The *tenderness in back* (Druckschmerz), which, according to Boas, is present in 30 per cent., has not been sufficiently tested in this hospital to warrant any conclusions.

Presence of Resistance or Mass. Out of 70 cases where this point is noted a mass was present in 20 per cent. and resistance in 14.2 per cent. The mass was in the right hypochondrium (36 per

cent.), epigastrium (29 per cent.), greater curvature (14 per cent.), pylorus (14 per cent.), and left hypochondrium (7 per cent.). The presence of a mass is often misleading, but the possibility of such, while not so frequent as in carcinoma, should always be kept in mind. In Osler and McCrae's[7] series of cases it was noted in 76.6 per cent.—only about three and one-half times more frequent than in our series. Reinhard has reported 16 cases with tumor in which simple ulcer was found at autopsy. The Mayos[2] have seen at operation 6 cases with tumor due to thickening about a chronic ulcer. Moynihan[8] in 100 gastroenterostomies for ulcer, found 10 cases with a tumor, 2 of which were thought to be malignant until the exploratory operation and subsequent course pointed to their benign nature. Gerhardt has described four conditions in which a mass may be present in a simple ulcer, viz.: 1. The thickened base and hard margin of the ulcer itself. 2. Functional hypertrophy of the musculature. 3. Localized exudate or abscess from perforation. 4. Adhesions between neighboring organs. There were examples of the three latter in our series. One case has been reported in detail by Osler[10] (Case 12) on account of the "prominent tumor at the pylorus, which relaxes and contracts and appears and disappears beneath the skin, due to the hypertrophied pyloric musculature."

Dilatation of the Stomach. This was present clinically in 18 out of 52 cases (34.6 per cent.); an absence of comment in the remaining 30 cases would warrant assuming the absence of dilatation. Therefore, a percentage of 22 would seem a fairer figure. As to the *degree*, it was marked in 7, moderate in 5, slight in 2, and not specified in 4. In the cancer series it was present in 42 out of 150 cases (21.3 per cent.). Broadbent has pointed out that extreme dilatation from carcinoma is rare. Osler and McCrae refute this, as they found a much larger number of cases of dilatation of the stomach due to malignant disease than any other single cause. Our figures place simple ulcer as *relatively* as frequent a cause, but on account of the greater prevalence of cancer in the Johns Hopkins Hospital, malignant disease would still take pre-eminence as a cause of gastrectasis. Dilatation in an ulcer signifies pyloric obstruction either directly from the ulcer, or scar, or perigastric adhesions, or indirectly from contraction or spasm of the pylorus from mechanical irritation. It must be remembered that there may be mechanical obstruction from contraction or spasm caused by a pyloric ulcer, *without* dilatation of the stomach (Hartmann's syndrome). The dilatation was determined by the tartaric acid and soda bicarbonate method *without* any harmful results. Hockman, however, has reported deaths from sudden distention of the stomach.

Gastric Analysis. The value of an elaborate analysis of the gastric juice is much exaggerated. We quite agree with Mayo that

the hydrochloric acid determination is the only one of value, and would add that *too much* importance cannot be attached to it. The Ewald-Boas breakfast is the one in vogue in this institution as elsewhere in America. The objection that exists in England to the use of the stomach tube in ulcer of the stomach does not prevail here. Unless there was a recent history of hemorrhage a test breakfast was given, and without any ill effects. To 53 patients a breakfast was given, and in only 1 case was a Riegel meal employed. Only 1 patient refused to submit. Of the 54 cases, no contents were recovered in 2. Analysis from one or more breakfasts was made in 52 patients; thus, 29 had one meal, 14 two meals, 5 three meals, 3 four meals, 1 six meals. Let us examine the results in detail.

Total Amount. Assuming that 40 to 50 c.c. be normal residue in one hour for the Ewald-Boas breakfast, and 300 to 350 c.c. at the end of two to three hours for the Riegel meal, there were 46 cases in which no figures were given, 54 per cent. above and 17 per cent. below normal, while the remaining 29 per cent. were within the limits of normal. It is interesting to note that many cases of Reichman's disease, where hypersecretion exists to an extreme degree, have been recently shown to be due to old cicatricial stenosis of the pylorus or duodenum.

Total Acidity. If we assume that normally after an Ewald test breakfast from 40 to 60 c.c. of decinormal sodium hydrate solution are required to neutralize 100 c.c. of filtered gastric contents, 27.5 per cent. of the cases showed hyperacidity, 42.5 subacidity, while the remaining 30 per cent. were within normal limits.

Free Hydrochloric Acid. This was tested qualitatively by Günzburg's reagent, and was found present in 82 per cent., and absent in only 18 per cent. of the cases. In 34 cases the quantity was estimated by tritration with dimethyl-amido-azo-benzol as indicator, which is undoubtedly less accurate than tropaolin. There was hyperchlorhydria in only 17.6 per cent.; the quantity of HCl was within normal limits in 26.4 per cent.; there was hypochlorhydria in 26.4 per cent.; in 1 case the free HCl was normal once, and below normal on the next examination. This is, however, in marked contrast with the results in our cancer series, where free HCl was absent in 92 per cent. These figures are rather contrary to the generally accepted statement that hyperchlorhydria is present in 75 to 80 per cent. of cases, as is held by Riegel and many others. Mayo[2] in a recent paper says "two facts are prominent, first, that 75 per cent. of gastric ulcers lie in the grinding apparatus of the pyloric end, and, second, that sometime in the history of gastric ulcer, and in the majority of cases at all times, there is a relative increase in the secretion of HCl, and, whether cause or effect, this excess is a most important etiological factor."

We repeat, our figures do not bear this out, nor have Ewald, Gerhardt, or Drechsfeld found such to be the case.

Lactic Acid. This was tested for in 43 of the cases, and was found present in 6 (14 per cent.), doubtful in 3 (7 per cent.), and negative in 34 (79 per cent.). In these 9 cases there was dilatation of the stomach in 4, subacidity without evident dilatation in 2, and neither dilatation nor subacidity in 3. In every case Uffelmann's reagent was used, but in only 2 was the juice previously extracted with ether. Let us glance at a brief summary of these 9 cases.

(*a*) *Positive Cases.* 1. Case 6.[28] Pyloric stenosis (cicatrix of ulcer); female, aged twenty-two years, colored, washerwoman; hospital No. 5646; admitted July 29, 1892. Absence of previous dyspepsia; sharp onset of symptoms of pyloric stenosis; marked emaciation; palpable tumor; dilatation of stomach with stagnation; test for lactic acid very positive on four occasions; that on August 22d, after daily lavage, showed lactic acid with absence of free hydrochloric. Operation; death; autopsy.

This case has been criticised by Boas as probably one of ulcus carcinomatosum. There can be no ground for this objection, as a careful gross and microscopic examination of the tissues was made. Dr. Thayer tells me, however, that the stomach was not washed out before each test breakfast as a preliminary precaution.

2. Case 15. Ulcer of the stomach; perforation with local peritonitis; hemorrhage. Male, aged forty-five years, piano-tuner; hospital No. 9473; admitted March 22, 1894. History of dyspepsia for six months, vomiting, but no hæmatemesis; marked loss of weight. No dilatation of stomach. Analysis of test breakfast on 23d instant showed no free HCl and no lactic acid, but vomitus of same date contained a faint trace. Readmitted on June 16, 1894, with a recent history of hæmatemesis. Test breakfast without previous lavage showed stagnation; faint HCl, and presence of lactic acid. Diagnosis on both admissions: cancer of stomach. Readmitted September 11, 1894, in a very grave condition; sudden death; autopsy.

3. Case 19. Gastric ulcer. Male, aged forty-eight years, cabinetmaker; hospital No. 11,250; admitted October 27, 1894. History of ulcer for four years. No dilatation of stomach. Test meals on the 29th and 30th show presence of HCl and also of lactic acid; latter disappeared two days later, though there was no note of gastric lavage; slight stagnation.

4. Case 34. Gastric ulcer. Male, aged forty-eight years; traveller; hospital No. 17,089. Admitted August 24, 1896. History of ulcer for twelve years. Test meal and specimen of vomitus give very slight reaction to free HCl and lactic acid. Stagnation slight. No note of previous lavage and no dilatation.

5. Case 36. Gastric ulcer. Male, aged forty-five years, laborer; hospital No. 18,427; admitted January 27, 1896. Ulcer history for two years; slight dilatation of stomach; only one test meal given,

which showed free HCl and slight reaction for lactic acid. Stagnation evident. No lavage. Discharged well.

6. Case 56. Cirrhosis of liver; cholelithiasis; ulcer of stomach. Female, aged forty-two years, laundress; hospital No. 31,023. Admitted June 27, 1900. History of cirrhosis of liver and alcoholic neuritis. No definite history of ulcer. Two test meals *after lavage* on previous night showed presence of blood and a definite reaction for lactic acid in ethereal extract. Readmitted on September 17, 1900, deeply jaundiced and comatose. No test meal. Death; autopsy.

(*b*) *Doubtful Cases.* 1. Case 10. Gastric ulcer. Male, aged thirty-seven years, oysterman; hospital No. 7743. Admitted July 20, 1893. History of ulcer for eight years; test breakfast on 21st showed free HCl and no lactic acid, but on the 25th instant good free HCl and a small amount of lactic acid. No note of lavage or dilatation. Discharged.

2. Case 30. Gastric ulcer. Aged thirty years, teacher; hospital No. 14,899. Admitted July 4, 1896. Ulcer history for two years; test meal on the 7th showed free HCl and a faint lactic acid reaction. No lavage and no dilatation. Discharged.

3. Case 54. Pyloric stenosis. Dilatation of stomach. Male, aged thirty-eight years, warehouseman; hospital No. 28,202. Admitted October 21, 1899. History of ulcer for nine months and stenosis for four; after previous lavage, on the 23d, there was no free HCl and a "suspicion of lactic acid," but on the 27th free HCl was found and no lactic acid. In spite of daily lavage, on November 7th and again on December 7th there was noted a suspicion of lactic acid and absence of free HCl. Operation; death; autopsy.

Hence it will be seen that in spite of gastric lavage before the test breakfast lactic acid was present in 2 cases—once on six occasions and once in small quantities on three occasions. In 3 of the cases daily lavage was performed without a disappearance of the lactic acid. In the other 4 cases there was no lavage instituted either before the meal or at regular intervals. We believe that the presence of the acid in these cases is due to stagnation of the gastric contents and a consequent fermentation, and in those 2 cases which still showed lactic acid, though after the prolonged use of lavage, the stagnation of even twenty-four hours was sufficient to account for the acid. Unfortunately we have no case illustrating the disappearance of the lactic acid with the relief of the stagnation by a more frequent use of the stomach tube. Lactic acid was present in 75.3 per cent. of the cancer series as contrasted with 14 per cent of our cases.

Blood was noted macroscopically in 18 out of 33 cases—in large amounts in 2, in small amounts in 7, in traces only in 2. In another 5 it was found microscopically alone. Thus, blood was present in 57.5 per cent. as compared with 26.6 per cent. of the cancer series.

Microscopic examination was recorded in 33 cases. It was negative in 18 instances. Red blood corpuscles were found in 8, red blood corpuscles and "bacteria" in 3, and bacilli in 4. The latter were in each case thought to be Oppler-Boas bacilli.

THE BLOOD. The alterations in the blood are those seen in any secondary anæmia due to hemorrhage—*i. e.*, of the chlorotic type. Rencki,[11] in 1901, after a careful study of the blood in 15 cases of cancer and 14 of ulcer, concluded that no characteristic differences could be made out between the anæmias of the two, and that examination of the blood is of very little value from a diagnostic point of view.

Red Blood Corpuscles. The red blood corpuscles were counted in 44 of our cases. The highest count was 6,784,000, the lowest 1,012,000, and the average of sixty-seven counts was 4,071,000 per c.mm. The highest count occurred in a patient (Case 67), who had almost constant vomiting, for which she was on rectal feeding for some time; the resulting concentration of the blood was the probable cause of the polycythæmia. The lowest count was in a case (Case 15) which was regarded on two previous admissions as cancer; indeed, it was not until the autopsy after the third admission that the true nature of the case was discovered. Where anæmia occurred it was due to hæmatemesis. In 1 case there was a difference of 4,332,000 per c.mm. between the count of the first and that of the third admission after a series of hemorrhages. There were 10 cases in which the red corpuscles were below 3,000,000, and 2 in which they were between 3,000,000 and 3,500,000 per c.mm. Osler quotes a case of duodenal ulcer with hemorrhage in which the red cells fell to 700,000 per c.mm. The average red count in Cabot's[12] series (51) was 3,372,000 per c.mm.; he states that "there is no single disease in which the red blood cells are apt to be so low, with the exception of pernicious anæmia." Greenough and Joslin report counts in 43 of their series, and in only 24 was the red count below 4,000,000 per c.mm. Grawitz suggests that the ulcerative process itself, *without* hemorrhage, may cause actual anæmia, but Cabot believes that it is uncommon to see marked anæmia in patients who have never had hæmatemesis.

White Blood Corpuscles. These were counted in 54 cases. The highest was 40,000, the lowest 1100 per c.mm.; the average of sixty-three counts was 7500 per c.mm. The leukocytosis of 40,000 (Case 15) is difficult to explain, unless it was due to the recent hemorrhage. Leukocytosis does occur under these circumstances, though usually to a less marked degree. Unfortunately there were no differential counts in our series. Digestive leukocytosis was tested for in 5 cases and was present in all, though never to a marked extent. The highest count was 10,500 per c.mm. The digestive leukocytosis is of very doubtful value in differentiating ulcer from cancer of the stomach, as has been pointed out by Osler and

McCrae, and later by Rencki. The former found it present in 10 and absent in 12 of their cancer series.

Hæmoglobin. This was estimated in 44 cases. The highest was 105 per cent., the lowest 12 per cent.; the average of sixty-two estimations was 58 per cent. The greatest variation in any one admission (Case 15) was 36 per cent. Cabot found the hæmoglobin reduced to a point below 50 per cent. in 80 per cent. of his cases. The average color index was 0.72, as compared with 0.67 of Greenough and Joslin. In the cancer series the average percentage of hæmoglobin was lower, being 49.9 per cent., while the color-index was 0.63. Hence the blood picture is that of a secondary or chlorotic anæmia, as seen from the following average determinations: red blood corpuscles, 4,071,000; white blood corpuscles, 7500; hæmoglobin, 58 per cent.

Urine. The pathological changes in the urine are not striking, and are usually accidental. Quincke says the urine is pale, abundant, and sometimes contains albumin. Albumin and casts were present in 15 of our series; a trace of albumin in 7. In 55 the urine was negative. In no case was there a quantitative estimation of the chlorides. Drechsfeld says the chlorides are often diminished and the phosphates increased. If dilatation be marked and fermentation increased there may be an excess of ethereal salts and indican. Acetone and diacetic acid were not noted.

Fever. This was present in 30 per cent. of our series. It did not exceed a degree or a degree and a half except in 6 cases. In 2 of these it was continuous, the ulcer being a complication of typhoid fever and pneumococcic septicæmia, respectively. In 4 other cases there was irregular fever, associated in three instances with complications—general peritonitis, tuberculosis, pyloric stenosis.

Complications. *Pyloric Obstruction.* Of the 76 cases of gastric ulcer there were 5 with definite pyloric obstruction and 1 doubtful case; 4 of these were confirmed at autopsy. There were also 2 cases of duodenal stenosis, both of which were confirmed at autopsy or operation. This gives 8 cases (9.7 per cent.) of obstruction from ulcer or its scar. There were in addition 10 other cases in which clinically the stomach was dilated, but no definite obstruction to its outlet was thought to exist. At autopsy the stomach was found dilated in 5 of these.

Deaths from Hemorrhage. Hemorrhage was the cause of death in 7 cases (8.5 per cent.), 1 of which was a duodenal ulcer. Of these, 4 were males and 3 females—*i. e.*, there was fatal hemorrhage from gastric ulcer in 4 out of 48 males (8.3 per cent.), and 2 out of 28 females (7.1 per cent.), the third case above mentioned having been one of duodenal ulcer. Our figures bear out the usual statement that hemorrhage is more fatal in the male than in the female. In the Boston series there were 5 males to 2 females. The ages of the males were forty-three, forty-five, forty-nine, and sixty-six, or an

average of 50.7 years; the ages of the females were ten and fifty, an average of thirty years. The case in which fatal hemorrhage occurred from a duodenal ulcer was in a girl, aged twenty-one years. That hemorrhage is relatively more fatal in the young female cannot be deduced from 2 cases. Hood, of London, in a period of twenty years at Guy's Hospital, found no case of fatal hemorrahge in a young woman. The latter is also supported by the Boston writers.

In all 7 cases the bleeding point was found at autopsy. In 2 other cases of gastric ulcer and 1 other of duodenal there was a profuse terminal hemorrhage with the gastrointestinal tract filled with blood, but no sign of a bleeding vessel was found.

Opinion as to the frequency of fatal hemorrhage is at great variance. Mayo Robson[13] says it is a very serious and common accident occurring in 7 per cent. Byrom Bramwell,[14] in his controversy with Robson on this point, stated that he had only 2 cases in his hospital or private practice in a series of 127 cases (1.57 per cent.), and was able to find only an incidence of 0.67 per cent. in the Edinburgh Royal Infirmary and 0.84 per cent. in St. Thomas' (London). Welch says it is the cause of death in from 3 to 5 per cent. The other authorities in numerical order are: Müller, 11 per cent.; Rodman, 8 per cent.; Steiner, 6.3 per cent.; Brinton and Debove, 5 per cent.; Drechsfeld, 3.5 per cent.; Lebert, 3 per cent.; Schulz, 1.7 per cent. The fatal nature of the hemorrhage depends upon the fact that the ulcer makes a lateral opening into the vessel, which prevents natural hæmostasis by the retraction and contraction of the artery. It is impossible to correctly estimate the size of the perforated vessel from the amount of blood or the length of survival of the patient. Robson[13] states that "capillary hemorrhage may be so free as to simulate rupture of a large vessel, yet after death a careful examination may fail to discover any gross vascular lesion. Dieulafoy has pointed out that severe hemorrhage may occur as the result of a "pore-like erosion" of the wall of one of the large branches of the gastric arteries without any marked ulceration of the surrounding mucous membrane, or, at most, accompanied by an abrasion so slight in degree that even at post-mortem the lesion may be overlooked (exulceratio simplex).

Hemorrhage may be capillary, venous, or arterial. The latter is the most common. Thus, Savariand, in a series of 54 cases, found ulceration of the splenic artery in 17, of the coronary in 6, pancreaticoduodenal, 7; gastric arterioles, 10; branches of the coronary vein, 2; other veins, 2; vessel not determined, 10.

In our series hemorrhage was from an erosion of a vessel in 6 gastric ulcers and 1 duodenal. In Case 15 the splenic artery was eroded, in another the arteria corona dextra, while in the remaining 5 it was a small arteriole or vein.

As to the *percentage of deaths* in gastric ulcer that are due to

hemorrhage, Bramwell gives 9.3 per cent.; Fenwick, 16 per cent.; Cordui, 20 per cent., and Welch, 27 per cent.

Exclusive of the 3 cases in which no bleeding point could be found, and in which hemorrhage was not absolutely proven to be the cause of death, there were 7 out of 24 deaths (29.2) due to hemorrhage.

PERFORATION. (*a*) *With General Peritonitis.* Only 1 case occurred in our series of 82 ulcers (1.2 per cent.), which is a remarkable fact when one considers that there have been somewhat more than 47,000 admissions in the past fifteen years to all services. The history of this case in brief is:

Case 40. Male, aged fifty-eight years, colored; hospital No. 19,664; admitted June 8, 1897, complaining of pain and vomiting; gastric symptoms for one year; acute onset four days before admission, with pain in upper abdomen and vomiting. No hæmatemesis and no melæna; great weakness and emaciation; collapse; signs of general peritonitis on admission; temperature, 100° to 103°; pulse, 120 to 132; respirations, 36 to 48. The case was considered inoperable by the surgeon, but after twelve hours there was some improvement and an exploratory laparotomy was performed. General peritonitis was present, and a small ulcer on the anterior wall of the pylorus was found, through which the gastric contents were exuding; the patient's condition was so bad that nothing further could be done, and death ensued shortly after the patient left the table. Only a partial autopsy was permitted, which revealed in addition to the perforated ulcer a small scar in its neighborhood.

(*b*) *With Localized Peritonitis.* There are two examples of this: one (Case 15) showed perforation through the posterior wall with localized abscess between the pancreas and the left lobe of the liver, evidently a gradual process of considerable duration. The second (Case 65) showed perforation of the posterior wall into the pancreas, which was considerably eroded and firmly adherent to the stomach. Including these 2 cases there was perforation of the ulcer in 3 out of 82 cases (3.6 per cent.), in 3 out of 24 deaths (12.4 per cent.). There was no case of perforation of a duodenal ulcer.

Greenough and Joslin found perforation in 3.2 per cent. in Boston. Pathological statistics exaggerate the frequency of perforation. The only trustworthy method is to observe the number of times that perforation occurred in a large series of clinical cases. Lebert found 3.5 per cent. of 252 cases; Fenwick, in 5.5 per cent. of 265 cases. Brunner has recently analyzed 380 gastric and 86 duodenal perforations, which have been reported between 1893 and 1903. He found that the accident occurs in about 2 to 4 per cent. of cases; it is more common in the gastric ulcer in England, and the duodenal in America. Only one instance was on record of perforation while the patient was at rest in bed under medical treatment; in another case it followed gastroenterostomy. Perforation is possible

in any situation in which ulcer may form, but is more frequent in the anterior wall near the pylorus and lesser curvature, or in the anterior wall of the upper horizontal portion of the duodenum. There is a certain small number of cases (7.5 per cent. of gastric and 20 per cent. of duodenal) in which perforation occurs without a previous history of ulcer. Brunner considers a diminution in liver dulness unassociated with tympanites characteristic of perforation of an ulcer; also that the site of pain is usually localized to the left of the median line in gastric and to the right in duodenal ulcer, and, further, that the area of tenderness in duodenal ulcer is not in the locality of the pain, but in the right iliac fossa.

Recovery from acute general peritonitis following perforation of a gastric ulcer may occur spontaneously. There are eight examples in literature.

Parotitis occurred in 1 case (1.2 per cent.), which has been reported in detail by Dr. A. Duval Atkinson.[17] A brief summary is as follows:

Case 29. L. P., female, aged thirty-five years; hospital No. 14,749; housemaid; admitted December 16, 1895, complaining of vertigo and general weakness. Family and personal history negative. For the past year has not been well, having continual pain in epigastrium, for one month, and amenorrhœa, for four months. On December 9th she took to bed because of gnawing sensation in epigastrium and nausea, and moderate hæmatemesis; latter was repeated in four hours, and was followed by extreme weakness. Examination on admission showed pallor of skin and mucous membranes; slight increase in cardiac dulness and a mitral systolic murmur; abdomen negative. Red blood corpuscles, 2,214,000; white blood corpuscles, 8000; hæmoglobin, 30 per cent. Urine had a specific gravity of 1010 to 1006, trace of albumin, and granular and hyaline casts. On December 16th there were pain and swelling of the left parotid, which by the next day had extended above the zygoma and far behind the mastoid, with infiltration of the side of the neck; locally redness, heat, and tenseness. On incision creamy pus exuded, which in cover-slips and cultures showed streptococci. No change in local condition, but patient gradually sank, and died on the 24th instant. There was no autopsy permitted.

This is not a very rare complication. Thus, Stephen Paget[18] reported 2 cases in 1897, and Hone[19] in the same year collected 8 cases from the literature and added 1 of his own. The latter was in a female, aged thirty-nine years, with a history of gastric ulcer for six years, with repeated hæmatemesis, who developed a double parotitis with little suppuration. Death; no autopsy permitted. This condition in ulcer is analogous to that found in injuries and diseases of the peritoneum, generative and abdominal organs. Some consider it more frequent in cases on rectal alimentation,

which is denied by Hone, who considers that hæmatemesis is a predisposing factor.

Tetany. We have only one illustration of this, which, though not recognized at the time, was probably tetany. It occurred in Case 29, reported above. This patient gave a history of "cramps" in the legs for one year, of the utmost severity, being of a shooting, darting character, coming on in paroxysms, and lasting several minutes. At the height of these pains a feeling of "pins and needles" would be felt in the hands and fingers. There was no evident gastric dilatation. It must be borne in mind that the milder grades of tetany may be overlooked entirely, such as muscular cramps and pricking in the extremities without typical contractures. When severe, tetany usually terminates fatally. Thus, Hochnard reported 10 deaths in 11 cases and Albu 31 out of 40.

Ulcus Carcinomatosum. There are 3 cases in this series in which cancer was supposed to have developed upon a pre-existing ulcer. Two of these (1 and 2) are very doubtful, and though diagnosed by the resident physician "carcinoma of the stomach (post-ulco)," they were considered merely cancer by Dr. Osler in his series. The history of these cases in detail is:

1. Case 26. Female, aged sixty years; hospital No. 12,287; admitted March 19, 1895, complaining of indigestion. For past year abdominal pain, worse after food and at night; vomiting of small amounts; hæmatemesis for two or three days one year ago; occasionally melæna; appetite good; bowels constipated; loss of weight. No tenderness, but mass to right of umbilicus; marked dilatation of stomach; analysis showed free HCl and total acidity of 77; discharged much improved.

2. Case 39. Male, aged forty-seven years, German, shoemaker; hospital No. 18,818; admitted March 6, 1897, complaining of "indigestion" for six years, and "vomiting," burning pain in perigastrium after meals, relieved by "knee-chest" posture; vomiting for four months, at first slight, now frequent, and large in amount. One attack of hæmatemesis four to five months ago, when on four or five occasions he vomited dark lumps of blood; loss of thirty-three pounds in weight; no tenderness; no mass; marked dilatation of stomach. Analysis gave a trace of free HCl and no lactic acid; hæmoglobin, 65 per cent.; red blood corpuscles, 6,120,000; white blood corpuscles, 8000. Patient discharged improved.

3. Case 64. Male, aged fifty-five years, colored, oyster shucker; hospital No. 33,849; admitted February 13, 1901. Patient was unconscious, and the history elicited from his wife did not point to the stomach. He died from a pneumococcus septicæmia, and at autopsy an old round ulcer was found on the lesser curvature of the stomach 7 cm. from the pylorus. Microscopic sections showed "in the depth of tissues glandular structures, in which epithelial cells are actually invading the surrounding tissue. This invasion is also to be seen

in the mucosa immediately adjacent to the ulcer." At first a diagnosis of "gastric ulcer with beginning carcinomatous change" was made, but Dr. McCallum, the resident pathologist, on re-examining the sections thought "that the slight new-growth of epithelium present is not more than might be accounted for in the regeneration process in the healing of the ulcer." There were no metastases or invasion of the surrounding tissue.

4. (This case was not included in our series, through an oversight.) Male, aged forty-nine years, painter; hospital No. 44,935; admitted December 7, 1903, for "stomach trouble." Past history negative except for syphilis in 1880. Present illness began three years ago with "heartburn" and acid eructation. In June, 1901, a profuse hæmatemesis from which he fainted, followed by tarry stools; frequent vomiting since onset, often very profuse; appetite good until nine months ago, when he gradually gave up solid food because of pain; loss of fifteen pounds in weight during the past five weeks; no emaciation or cachexia. Local tenderness in epigastrium; active visible peristalsis and marked dilatation of stomach; firm, nodular mass to right of mid-line and 3 cm. above umbilicus. Hæmoglobin, 45 per cent.; red blood corpuscles, 3,004,000; white blood corpuscles, 15,200. Test breakfast showed marked hypersecretion and hyperchlorhydria (100.5), with blood-streaked mucus. The hyperchlorhydria practically decreased with gastric lavage, until by December 18th there was a marked subacidity. There was always a morning residue of 400 to 2000 c.c. The general condition improved; there was a gain of two pounds in weight, and the blood rose to 60 per cent. hæmoglobin and 4,000,000 red blood corpuscles. The patient was transferred to the surgical side, and an operation was performed December 30, 1903. At the exploratory operation there was marked dilatation of the stomach, with a mass surrounding the upper two-thirds of the pylorus. Several large, hard glands were found, one of which was very suspicious on section. The mass itself was thought to be carcinoma, which was afterward confirmed by the pathologist. Pylorectomy with gastrojejunostomy was done. The patient made an uninterrupted recovery, and when last heard from, six months ago, was doing well.

Let us consider the pros and cons in these 4 cases. In the first there is no definite ground for the supposition of a pre-existing ulcer; as the onset with hæmatemesis one year before is not against a beginning cancer. In the second, the history of "indigestion" for six years *suggests* the possibility of ulcer, but the recentness of the hæmatemesis (fifteen months) and the vomiting (four months) all point to a developing carcinoma. In the third case we have no previous history to aid us, and the most we can say is that there was an old ulcer which might have developed into cancer if the patient had survived, but was not definitely malignant at the time of his death. The fourth case is undoubtedly one of carcinoma, which,

from the preceding history, probably developed upon an old ulcer, though from the size and character of the mass the early symptoms might have been due to a slow growing scirrhus cancer.

Hence in our series there are only 3 out of 82, or, better, 4 out of 83 cases (4.8 per cent.) in which there is any reasonable possibility of a simple ulcer having developed into a malignant one. Fenwick found only 2 out of 89 ulcer cases (2.2 per cent.) which showed evidence of malignancy. Contrary to our belief, there are many who consider that a large proportion of cancers of the stomach develop from a pre-existing benign ulcer. Riegel believes it to be a frequent occurrence, while Zenker maintains that the majority of carcinomata originate from ulcer. According to Lebert 9 out of every 100 cases of carcinoma of the stomach are due to ulcer. Graham,[2] Mayo's associate, found in 135 cases of cancer an ulcer history in 60 per cent. Rosenheim found such a history in only 6 per cent. of the cancer cases, and Barling and Hirschfeld in but 5 per cent.

Sticker pointed out that in those rare cases of carcinoma in which free hydrochloric acid persisted the origin was in a benign ulcer.

Associated Conditions. These are numerous. Tuberculosis occurred in 4 cases; in two the involvement was of the peritoneum and lungs, and in two general. Cirrhosis of the liver was present in 3 cases and obscured the clinical diagnosis, the hæmatemesis being ascribed to a ruptured varix. Jaundice was present in 2 cases from involvement of the gall-ducts in adhesions: in 2 further cases gallstones were found. It is interesting to note that Case 75 was at first thought by the family physician to be one of gallstones on account of the site of the pain; the subsequent diagnosis, however, was cicatricial stenosis of the pylorus. At the exploratory operation the cicatrices were found to be in the duodenum. The patient is now perfectly well. Two cases were complicated by aneurysm of the aorta, 1 of these died from hemorrhage from erosion of a vessel in the gastric ulcer. Two patients had chronic nephritis, and 2 had arthritis deformans. What part these processes played in the etiology is difficult to estimate. There were many other associated conditions (erysipelas, strangulated hernia, pyosalpingitis, etc.). The most important one was typhoid fever, in the course of which sudden pain in the epigastrium and profuse hemorrhage with signs of peritonitis led to an exploration for "perforation," with negative result. One day later, at autopsy, an acute gastric ulcer, with erosion of a vessel, was found.

Duration and Course. The chronicity of the disease is well recognized. The usually accepted time-limit is from three to five years. Sixty-four of our cases had suffered from periods varying from two months to twenty years, the average being 4.1 years. Cases are on record of longer duration. Thus, Habershon reports a case of forty-six years, and Brinton one of thirty-five years' dura-

tion. Lebert found ulcer to be latent in 15 per cent.; of less than one year's duration, 18 per cent.; one to six years, 46.5 per cent.; six to twenty years, 18 per cent.; and twenty to twenty-five years, 2.5 per cent.

TREATMENT. *Medical Treatment.* The treatment followed in the medical wards is similar to that in vogue elsewhere. First of all, absolute bodily rest is insisted upon for a period of from three to six weeks. The stomach is given either complete rest (*i. e.*, rectal feeding for a period varying from five days to two weeks, according to the severity of the case), or partial rest is afforded by the blandest diet—thin soups, whey, milk, etc. Some clinicians, as Fournier, insist upon rectal alimentation for two weeks or even one month. The bowels are regulated, and the anæmia, if present, treated by iron or arsenic. The hyperacidity is counteracted by large doses of carbonate of magnesia, and occasionally by gastric lavage. This latter was instituted in a few cases only, but with marked benefit, even in those without dilatation or obstruction.

Surgical Treatment. The indications for surgical treatment, according to Mayo Robson, are: 1. Perforation. 2. Perigastric adhesions, as pyloric obstruction or hour-glass stomach. 3. Ulcer, intractable to prolonged medical treatment. 4. Recurring and profuse hæmatemesis. 5. Certain cases of acute hæmatemesis.

Let us consider these various indications:

Perforation. All now are agreed upon the advisability of immediate operation for this fatal complication. The great strides that have been made in this branch of surgery are very encouraging. Thus, Weir and Foote, in 1896, gave the mortality in perforation cases treated surgically at 71.5 per cent., while four years later Tinker[20] found that it had dropped to 42.6 per cent.—indeed, in those operated upon in the first twenty-four hours the mortality was only 25 per cent. Mayo Robson[21] in the same year in 429 collected cases found the mortality to be 35 per cent. Brunner,[16] in 1903, gave the mortality as 48 per cent. in gastric and 80 per cent. in duodenal. Of course, statistics collected from literature give an exaggerated idea of the good results of operation, as the majority of the favorable cases are published; nevertheless, the mortality from perforative ulcer is becoming rapidly less—in direct ratio to the number of cases that are early handed over to the surgeon.

Hemorrhage. In this hospital only one case of hemorrhage from gastric ulcer has been treated by the surgeon. This was Case 62 (the typhoid fever patient), who had developed sudden abdominal pain, hemorrhage, and signs of perforation, but in whom the source of the bleeding was, however, not discovered until after death. Dieulafoy[15] advises surgical intervention, if the hemorrhage is as much as half a litre, and *insists* if the bleeding is repeated in twenty-four hours. Moynihan[22] divides the cases into two classes: 1. Acute ulcer, in which operation is *not* indicated except in a few

cases where hemorrhage is both copious and recurrent. 2. Chronic ulcer, where operation is indicated in (*a*) a group of cases where bleeding is copious and transient, and (*b*) frequent recurring hemorrhage, which is now and then profuse.

While concurring for the most part with the previous writers we cannot agree with a recent statement[23] that "it would appear justifiable to perform gastroenterostomy in every case of gastric ulcer in which, in addition to the other clinical data, gastric hemorrhage is observed." Rodman collected, in 1900, 32 cases of acute gastrorrhagia, with 40.6 per cent. mortality, and 31 cases of chronic gastrorrhagia, with 19.3 per cent. mortality. Mayo Robson,[21] in 1900, found a mortality of 64.2 per cent. in operative cases, as compared with 5 to 10 per cent. treated medically. Moynihan,[8] in 1904, quotes 1 death in 15 cases treated for acute or recurring hemorrhage (6.6 per cent.). Robson, we believe, takes the more conservative stand when he states that medical and general treatment is successful in arresting hæmatemesis in 93 per cent. of the cases, hence should be given a fair and complete trial for at least a few hours.

In the small number of cases where surgical intervention is advisable, Finney's gastroduodenostomy or a posterior gastroenterostomy seems the operation of choice.

Perigastric adhesions were present in 11 of the 23 gastric cases at autopsy or operation (48 per cent.), and in 3 of the 4 duodenal cases (75 per cent.). According to Robson, these are present in 5 per cent. of all necropsies and in 40 per cent. of gastric ulcer cases. Hale White[25] gives the figure in the latter case at 45 per cent., while Fenwick found the stomach adherent in 46 per cent. White has outlined the points in the diagnosis of this complication. There is present very severe pain, more or less constant, not increased by food, though often paroxysmal, and often persisting for years. Dilatation of the stomach or symptoms of gastric ulcer may or may not be present. Vomiting or emaciation may be absent, as the digestion is good. Local tenderness or even an indefinite mass from matting together of the viscera sometimes occurs. In such cases operative measures should be undertaken. White succeeded in curing 3 out of 5 cases.

Comparison between Surgical and Medical Results. Hardly a sufficient number of cases treated by surgical interference have been followed for a sufficient period to justify a comparison with the results of medical treatment. Mayo Robson had a mortality in 1901 of 5 per cent; W. J. Mayo, of Rochester, Minnesota, 6.5 per cent.; Peterson and Merchol, 11 per cent. Moynihan, in 1904, among 100 cases treated by gastroenterostomy alone, had a mortality of but 2 per cent. These figures all compare favorably with those resulting from medical treatment, the mortality of which varies between 10 and 20 per cent.

The 82 cases treated in the Johns Hokpins Hospital may be tabulated as follows: died, 24 (29.3 per cent.); well, 14 (17.1 per cent.); improved, 39 (47.6 per cent.); unimproved, 3 (3.6 per cent.); not treated, 2 (2.4 per cent.). The term "well" was applied only to those cases which had been free from all symptoms of ulcer for a sufficient time to warrant the hope that the disease was arrested. The large number of deaths (29.3 per cent.) is difficult to explain until one realizes that 11 of these cases were not treated for the ulcer, but died from some intercurrent affection, the ulcer being recognized only at autopsy. The mortality of 69 treated cases was 13, or 18.8 per cent. Cordier says that ulcer is four or five times more frequent in women than in men, but that the mortality during the latter is much greater. In our series there were 16 deaths among the males to 8 among the females—*i. e.*, the proportion was 2 to 1, which, however, corresponds to the incidence in our series, so that the mortality in both series is practically equal. Of the 58 cases that left the hospital during the past fifteen years we sent out a circular letter and received replies from twenty-six, while eleven letters were returned unclaimed.*

The after-result of these twenty-six for an average period of five years is seen in Table IV.:

TABLE IV.

At discharge.		At an average of 5 years.			
		Recurrence.	Death.	Well.	Total.
Died,	24 = 29.3 per ct.	0	0	0	0
Well,	14 = 17.1 "	4	2	5	11
Improved,	39 = 47.6 "	3	4	8	15
Unimproved,	3 = 3.6 "	0	0	0	0
Not treated,	2 = 2.4 "	0	0	0	0
Total,	82	7	6	13	26

* CIRCULAR LETTER.

DEAR .....

We are interested to know what your condition has been since discharge from the hospital in . Will you kindly answer the following questions:

1. Pain in stomach, if any?
   a. Location.
   b. Character of pain.
   c. Relation to food.
2. Vomiting, if any?
   a. Amount, large or small.
   b. Vomiting of blood, quantity, dark or bright.
3. Passage of blood in stools?
4. Have you been in any hospital since discharge from Johns Hopkins? If so mention hospital and about date of admission.
5. If patient be dead will nearest relative kindly report from what cause and under whose care (physician or hospital)? Were symptoms of stomach trouble still present?

Yours truly,

.....

In other words, of 26 patients since discharge there have been 6 deaths (23 per cent.), 7 recurrences (26.8 per cent.), and 13 permanent cures (50 per cent.) for periods ranging from six months to thirteen years. Of the 6 deaths, the cause was gastric in 2, non-gastric in 2, and unknown in 2. Greenough and Joslin publish 55 per cent. cured, 25 per cent. relieved, 13 per cent. dead, and 6 per cent. otherwise at discharge. Their after-results are seen in Table V.:

TABLE V.—GREENOUGH AND JOSLIN'S 114 CASES.

	At discharge.	Recurrence.	Death.	Cure.	Total.
Cured,	63 = 55 per ct.	28	8	27	63
Relieved,	29 = 25 "	10	4	15	29
Deaths,	15 = 13 "	...	...	...	15
Otherwse,	7 = 6 "	3	3	1	7
Total,	114	41	15	43	114

The latter table shows recurrence in 50 per cent. as compared with 85 per cent. of Welch, 74 per cent. of von Leube, 75 per cent. of Ewald, and 50 per cent. of Debove.

Russel,[25] of Birmingham, followed the after-history of 63 cases in females, and found that after a period of two years there was a direct mortality in 2.1 per cent. Recovery in 42.6 per cent. and recurrence in 44.7 per cent. Schulz[27] followed 88 cases of ulcer treated medically, in all of which hæmatemesis was present, and found that there were 9 per cent. deaths and only 64 per cent. permanent cures.

Of our 58 cases of gastric ulcer that received medical treatment, 11 were discharged well, 38 improved, 3 unimproved, and 5 dead—*i. e.*, a mortality of only 8.6 per cent. Eleven cases have been transferred for operation, which is too small a number for comparison with the above.

MORBID ANATOMY. For observation we had 23 cases at autopsy and 4 at operation. 23 were gastric and 4 duodenal.

CONDITION OF THE ULCER. The ulcer was more or less active in 19 cases of gastric ulcer and 3 of duodenal. Cicatrization had occurred in 3 gastric and 1 duodenal. In 1 case the condition of the gastric ulcer was not stated. That is to say, there were 22 ulcers to 4 scars—a ratio of about 5.5 to 1, rather contrary to Welch, who considers that the scar is at least twice as frequent as open ulcer.

As to the *number*. In 20 cases—16 gastric and 4 duodenal—there was but one ulcer; in 1 case there were two ulcers; in 1 three ulcers, and in 3 (11.1 per cent.) there were several ulcers. Brinton believes that multiple ulcers are found in 20 per cent.

The particulars as to the site, presence of adhesions, local or general peritonitis, etc., are given in detail under the various clinical sections.

CONCLUSIONS. 1. Gastric ulcer is rare in the Johns Hopkins Hospital as compared with cancer, the respective incidences being 1 to 225 and 1 to 56 general admissions.

2. Gastric ulcer in our series was as common in the male as in the female. In the male the percentage of greatest frequency was between the ages of forty and fifty—a decade later than usual.

3. Ulcer was in our cases relatively more frequent in the colored race and among Germans.

4. Vomiting occurred in 85.3 per cent.; pain in 82.9 per cent., and hæmatemesis in 75.6 per cent.

5. Great loss of weight may be present; thus, in 36 cases there was a loss of more than ten pounds, and in 9 of forty pounds or more.

6. Our statistics would indicate that hyperchlorhydria is not so constant as usually maintained; it was present in only 17.6 per cent. of our cases.

7. The blood picture is one of chloranæmia as seen from the average count (hæmoglobin, 58 per cent.; red blood corpuscles, 4,071,000; white blood corpuscles, 7500 per c.mm.).

8. Hemorrhage was the cause of death in 8.5 per cent. of the total number of cases, and in 29.5 per cent. of the fatal cases.

9. Perforation is rare (3 cases, or 3.6 per cent. of our series). General peritonitis occurred in but one instance (1.2 per cent.).

10. Ulcus carcinomatosum is rare—at least 4.8 per cent. of our series.

11. Operation is indicated in all cases with perforation or perigastric adhesions, and in cases of copious or recurring hemorrhage, when medical means have failed after a fair trial.

12. The mortality of the series was 29.3 per cent.; in the cases, however, who received treatment there was a mortality of only 18.8 per cent.; in those receiving medical treatment alone, 8.6 per cent.

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INTERMITTENT HYPERCHLORHYDRIA AS AN OCCASIONAL CAUSE OF RECURRENT VOMITING IN CHILDREN.

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The object of this paper is to direct attention to the curious symptom-complex called cyclic, periodical, or, better, recurrent vomiting of children, with the idea (1) that the condition is not as rare as is generally supposed; (2) that it is relatively easy of diagnosis, an examination of the vomited matter being most important; (3) that at least in some cases the gastric irritability is due to an intermittent hyperchlorhydria, a secretory neurosis, causing the sudden hypersecretion of free HCl and gastric juice.

Vomiting is the main symptom of the malady. The subject, except for the attacks, is in perfect health. The vomiting attacks occur at irregular intervals, begin with slight premonition, continue usually a few days, and cease suddenly, leaving the patient with an unimpaired appetite and digestion.

A similar group of symptoms has long been recognized in adults. In mature life gastric pain is a most prominent feature, while children suffer more from nausea.

The condition in children was first recognized by American authors, although a suggestion as to its existence was first published by Gee. In 1893 I attended a little girl who was harassed by repeated and dangerous attacks of vomiting, lasting several days, and appearing without adequate exciting cause or dietetic error. I reported the case, under the title of "A Gastric Neurosis in Childhood," to the American Pediatric Society. An interesting discussion followed, showing that many of the members had seen these repeated prostrating attacks of vomiting, that they did not consider them ordinary gastric indigestion or gastritis, as they appeared suddenly in children with normal digestion, carefully fed, and the illnesses terminated abruptly, and were separated by intervals of perfect health.

Since then numerous cases of recurrent vomiting have been reported, and the condition is mentioned in most English and Amer-

ican text-books. Either the disease is rare or unrecognized in Germany, as Heubner in his new book entirely ignores it.

An explanation as to its cause has been diligently sought, principally through urinary analyses, and in my opinion no satisfactory theory as to its etiology has been advanced. Probably several phases of disturbed or faulty metabolism may provoke the vomiting.

Marfan gives an accurate description of the condition under the title of "vomiting and acetonuria." He evidently regards it of common occurrence, as he cites twenty-five personal cases. He found the vomiting associated with the odor of acetone in the breath and acetone in the urine, and regards the malady as the result of an intoxication, the acetone being the witness or companion of the toxic product. The expression of the malady is through the stomach, giving rise to persistent and dangerous vomiting.

Edsall believes that recurrent vomiting is sometimes the result of an acidosis, a cryptogenic acid intoxication analogous to the fatal intoxication seen in diabetic coma and other exhausting diseases. His proof is that the odor of acetone is present in the breath and that acetone, diacetic acid, and oxybutyric acid are present in the urine, but only during an attack. The acetone is not the cause of the symptoms, the vomiting being due to the presence of an excessive amount of acid, producing a reduction of the alkalinity of the tissues and body fluids and the loss of alkalies in the excretions, the acids carrying off the alkalies in combination.

Edsall recommends giving large doses of a soluble alkali at the beginning of an attack, to combat the acid intoxication, and certainly his treatment is the most effective known, as the vomiting resisting all other known modes of treatment will occasionally disappear or be prevented, after the administration of large doses of bicarbonate of soda.

Rachford found poisonous leukomaines in the urine, and believes the condition a lithæmic gastric neurosis, allied to migraine. In his cases the vomiting disappeared and was replaced by migraine in adolescence. It may be remembered that migraine is often caused by hyperchlorhydria.

Holt regards recurrent vomiting as a nervous explosion, analogous to migraine in the adult, due to faulty metabolism.

It is to me remarkable, in an illness whose main symptom is vomiting, that so few accurate analyses have been made of the vomited matter. Testing the ejecta would seem to me to be the clue to correct diagnosis and treatment. However, Holt reports the usual findings as of a fluid containing mucus and free HCl. In four of my personal cases the fluid vomited was apparently pure gastric juice, containing an excess of free HCl and mucus, and in the fifth case the hyperacidity was due to combined chlorides.

It is, therefore, probable that *some* cases of recurrent vomiting are the result of an intermittent form of hypersecretion of highly acid gastric juice.

If recurrent vomiting in chlidren is sometimes due to a sudden hypersecretion of irritating gastric juice, the symptoms are far more dangerous and prolonged than in analogous conditions in adults. The free HCl primarily causes spasmodic contractions of the pyloric valve, increased peristalsis of the stomach walls producing gastric distress, nausea, and frequent vomiting. Often blood is mixed with the ejecta, due to traumatism of the stomach walls from violent retching. The vomiting is followed by rapid emaciation, great cardiac weakness, and on rare occasions death.

The disease usually begins in early childhood, from the first to the sixth year. All of my cases were of the better class of society—nervous, high-strung children of average physique. None of them had been debilitated by any exhausting malady. All were fed with an excess of caution. In none was there any flagrant dietetic error. The prodromal symptoms were insignificant—languor and slight fever. Many of the attacks arose out of a clear sky, beginning suddenly, with no adequate cause, ending abruptly, leaving the digestion undamaged, with weeks or months of excellent health.

I will give short histories of five of my personal cases. All were girls. Of 20 recorded cases, 12 were girls, 8 boys.

Case I.—Margeret R. Both parents in good health. A baby sister died at fifteen months, after several days of uncontrollable vomiting.

Child born on October 20, 1899; suckled eleven months. After weaning there followed a period of anorexia, lasting four months. During this time the baby would not take food from a bottle, cup, or spoon, nor suckle a wet-nurse. For four months the father, a physician, laid the baby on its back, held its hands, and forced down food into its mouth with a large pipette, the child meanwhile expressing its aversion to its meals in the most violent manner. It digested what it swallowed, and slowly improved. At three years it was brought to the city in superb health after a summer in the country. In a week she had an attack of vomiting lasting forty-eight hours. During that time there was a temperature of 101°, a slightly coated tongue, and very abrupt cessation of all symptoms, save there was mucus in the stools for a few days.

After this the illnesses recurred every six to eight weeks. The little girl would go to bed perfectly well, would commence vomiting at night, and would vomit every half-hour to two hours until the attack terminated, usually two to three days, absolutely nothing being retained in the stomach. During the illnesses there was thirst. The temperature was 100° to 101°, the tongue gradually becoming more coated. The skin and breath had a curious fruity odor—acetone. The abdomen was never tender, but always

retracted, the contour being due to empty intestines and general asthenia. The bowels were constipated; an enema would bring away a well-digested stool. The vomited matter was, first, food debris, later one to two ounces of pure gastric juice. In an attack periodically the child would become restless from gastric distress, would vomit, and be easy for a while. Suddenly the child would look better, and take and retain its ordinary meals. In spite of a restricted diet and semistarvation, the attacks continued and grew worse. One in April lasted four days. There was noticeable emaciation and exhaustion; the pulse was weak and irregular; sighing respiration and cold extremities. Urine examined; no albumin, casts, or sugar.

In May, 1903, occurred the worst and final attack. I saw the child after it had vomited two days. The surface was cold. Temperature 102°; pulse 160, very feeble; patient delirious; there was a noticeable odor of acetone in the breath. The vomiting was projectile; the ejecta contained mucus and streaks of blood. The girl was in a dangerous condition of cardiac weakness from inanition and protracted vomiting. An examination of the ejecta showed it to be gastric juice, acidity 18, due to free HCl; mucus, blood, and shreds of the stomach walls were also present. A hypodermic of strychnine was given, and first 10 grains and later 20 grains of bicarbonate of soda in water every hour by the mouth. After the alkaline treatment, vomiting occurred only once (200 grains of bicarbonate of soda were given in twelve hours). A remarkable amelioration was soon seen in the child's general condition. The gastric distress ceased, the odor of acetone disappeared, the skin became soft and warm, and the next day she was put back on her usual diet. The urine continued acid until the second day, although 400 grains of soda were given in thirty-six hours. For eleven months this child was given soda in sufficient doses to keep the urine slightly acid. One day in the winter she vomited for a day. The doctor gave 20 grains of soda every hour, and fed her beef-juice and malted milk. The food was retained; the vomited fluid was hyperacid gastric juice. No real recurrence has taken place in eleven months. To my regret no examination of the urine for acetone or diacetic acid was made, but the odor of acetone was evident in the breath.

This is a case of Edsall's acid intoxication causing a hypersecretion of gastric juice. The alkaline treatment was brilliantly successful in arresting the vomiting and preventing a recurrence for nearly a year.

Case II.—Helen S., daughter of a physician. Pertussis at three years; at five years developed a craving for bicarbonate of soda, asking for it and preferring it to sweets. During the summer of 1903 she was in good health, eating freely of fruits.

In September, 1903, while taking a drive, she began to cry, and vomited half-digested food. Temperature at first 99.6°, later

normal. The vomiting continued four days. During this time the child was much distressed from nausea, and threw up every hour one to two ounces of bitter, greenish or yellowish fluid containing mucus, and on two occasions blood. The tongue was coated, and the breath had the odor of a sour stomach; abdomen retracted; bowels moving only after enemata. In the last two days the patient sunk into a condition of grave prostration, with a rapid, weak pulse. Ten pounds of flesh were lost in this illness. After the retching ceased the child had a ravenous appetite, and digested well a very restricted diet.

October 25th. For no apparent reason the vomiting recurred and lasted seventy-two hours. The father noticed much more liquid was vomited than was swallowed.

January 5th. Another attack lasting four days. The illness was characterized by paroxysms of intense abdominal pain, relieved by vomiting. On the fourth day the child was carefully examined. There was no odor of acetone in the breath. The ejecta contained no free HCl; total acidity 40, due to combined chlorides. In exceptional cases with symptoms of hyperchlorhydria the gastric contents show a high acidity due to combined chlorides, not to HCl.[1] The father gave a heaped teaspoonful—90 grains—of sodium bicarbonate at a dose in water every one and one-half hours; vomiting occurred only once after the alkali. (In this case the soda was given in too large a dose and might have irritated the stomach.)

February 10th. Urine analyzed in a period of apparent health; acetone present; no diacetic or oxybutyric acid, showing very clearly that the acetone in this case was not due to inanition from an exhausting malady, but was a premonition of an impending systemic intoxication. I told the father the girl would soon be sick again, and going back to lunch he found her crying from pain in her stomach. He gave her a large dose of soda, and the distress disappeared. From February 10th to March 18th he kept the urine alkaline. On March 18th the father was ill with la grippe, and soon after the daughter sickened, with hoarseness, nasal discharge, and fever. On the third day the influenza was complicated by frequent vomiting, lasting four days. The acidity of the stomach contents was 40, due to combined chlorides; no free HCl. The vomiting was not relieved by soda, which was again given in too large a dose. On her recovery the child was taken to an oculist, who found some error of refraction and put on glasses. There was so much anæmia and debility from this illness that the child was taken South.

In this case the gastric irritability was due to combined chlorides.

CASE III.—Helen W., aged nine years, always constipated in sickness and health; otherwise, a well-developed, handsome girl. In infancy was fed on peptonized milk and suffered from consti-

[1] Stockton, p. 315.

pation, colic, and a slow gain in weight. First attack of vomiting, lasting seven days, occurred at two years of age from improper feeding. From that time, with the exception of her sixth year, she has had vomiting, attacks lasting from two to fourteen days at intervals of six to twelve weeks. Diet made no difference in preventing attacks; between them her digestion was perfect. Her illnesses were more frequent in winter than in summer. They were occasionally precipitated by fatigue after a long walk. They would sometimes cause alarming prostration. The family physician said the vomiting was always preceded by aggravated constipation.

July, 1903, was spent at the seashore; the patient grew strong and vigorous. Immediately on her return she was sick, and vomited thirty times in eighteen hours. The attending physician gave 10 grains of soda every hour, but the remedy apparently irritated the stomach and increased the retching. Recovery was slow, and the child would not eat for a number of days. After this 10 grains of soda were given three times a day. She was vaccinated in November and vomited for a day.

December 19th. The child began vomiting at 7 A.M.; given 10 grains of soda every hour. Emesis at 7, 8.15, 9.15, 9.45, 10.35, 11.15, 11.56 A.M.; 12.35, 1.05, 1.35, 2.15, 2.55, 3.20, 4, 5.40, 6.30, 7, 7.45, 8.55, 10.35 P.M.

20th. 12.15, 1.15, 5.30, 8.20, 10.45 A.M.; 1.35, 2.30, 3.55, 5.45, 7.05, 7.20, 8.20, 9.20, 9.40, 10.45 P.M.

21st. 12.30, 1.30, 2.30, 2.46, 4.05, 5.05, 5.25, 6.30, 6.50, 7.40, 8.50, 9.40, 10.40, 11.40, 12 A.M.

22d. 1, 1.30, 2, 2.30; attack ceased suddenly at 2.30 A.M. Vomited forty-one times in sixty-seven and one-half hours.

I saw the patient on the third day of the illness at 4 P.M.; rectal temperature 100°; skin cold and clammy; dark circles under the eyes; tongue slightly coated; abdomen retracted, not tender; no odor of acetone to the breath; heart action fairly strong (135); urine scanty. The child was thirsty; always threw up the water swallowed. In fact, it made no difference in the vomiting whether anything were taken or not there was much nausea. The ejecta consisted of an acid, milky colored fluid containing free HCl. Urine contained no albumin, casts, or sugar; not examined for acetone.

The last attack occurred in February. The patient vomited continually for ten days, then a lull of a few hours, in which food was given; then it began again and lasted eighteen days, until her life was despaired of. Her convalescence was so slow that she remained in bed a month. This is the longest and most severe attack I have knowledge of that did not result in death. The alkali was persistently given in suitable doses, but gave no relief. We were never even successful in neutralizing the acidity of the ejecta. The only ray of comfort was given by hypodermics of morphine, which

strengthened the heart and gave some slight respite from the frequent retching.

CASE IV.—Ruth N., an active, very intelligent, and emotional little girl. During infancy she was nursed, but from the age of one month she would often become feverish and vomit continually from twenty-four to seventy-two hours. These attacks were never preceded by constipation or prevented by the most rigid diet. After infancy they were often associated with sore throat. At the age of four and one-half years nasal adenoids were removed. During the summer of 1902 there were two attacks, when every hour or two she would throw up a quantity of clear, sour-smelling, watery fluid mixed with mucus. The child lay motionless in bed, refusing to swallow or to stir. She would literally get well in a minute, go out, eat, and enjoy herself.

Description of Two Attacks.

September 28th. She sickened in the night, with a temperature of 104°, pulse 150, vomiting, headache, and sore throat; the pharynx was not inflamed; bowels moved in the early morning. After forty-eight hours the little girl became much prostrated by her symptoms. The mother took the child out-of-doors at midnight; the nausea disappeared, and she called for food, slept, and was well again.

December 27th. Child languid, complained of headache; temperature 104°; from 6 A.M. to 10 A.M. vomited three times; 10 A.M., pulse 165, temperature 101° at 4 P.M.; the little girl was smiling; vomit matter examined; hyperacid gastric juice; total acidity 10, due to free HCl; 0.365 per cent. of free HCl.

The vomiting did not return, but the patient suffered for a week with fever and left-sided torticollis.

In March, 1903, child had an attack of whooping-cough, in which malady, strange too, although vomiting is expected, it did not occur. This would indicate that these gastric crises were not due to any abnormal stomach reflex, but to some central nervous irritation or intoxication stimulating the centres governing the secretion of HCl. This case is rather atypical, as the gastric crises were associated with high fever. There was also a strong psychical element, as the vomiting would occasionally stop suddenly, by a pleasurable sensation, by the appearance of the father with a new toy, or if the child were taken into the open air.

CASE V.—Katharine C., aged eight years; a very neurotic family history; grandfather and father alcoholic; mother suffered from eclampsia in infancy; an elder sister died of epilepsy; two brothers had infantile convulsions. The little patient herself was rachitic.

First manifestation began at nineteen months, with a convulsion, followed by slight fever and the frequent vomiting of a thin, acid

fluid for five days; sudden cessation of vomiting and restoration of digestion.

Eleven months later a second attack, ushered in by a convulsion, with fever and vomiting for five days, causing grave exhaustion. After this the eclampsia ceased, but the vomiting attacks continued at intervals for two years. Once she brought up a large quantity of fresh blood. She would barely recover from an illness before another commenced.

In January, 1893, I first saw the case. She had had the usual symptoms for ten days, and her parents were alarmed at her dangerous weakness. Temperature 101.5°, pulse 120. Pulse and respiration regular; tongue slightly coated; abdomen not tender, markedly retracted; rectal examination negative; one stool in ten days.

The gastric irritation seemed to recur periodically; there would be a burning in the stomach; nausea. The child would swallow water, and immediately vomit a very acrid fluid.

She was a slender, undersized girl, not emotional, save for these gastric crises; appetite, digestion, and stools were perfect. All the medicine and food that I ordered were vomited. On the fourteenth day the symptoms disappeared, and she ate and slept and played as usual.

In seven weeks another attack occurred, precipitated by a puzzling lesson in subtraction. The vomited matter was pure gastric juice, containing an excess of free HCl. Alkalies did not relieve the symptoms nor neutralize the acidity. The vomiting was evidently due to a recurring hypersecretion of gastric juice, irritating the stomach and pylorus. She was given large doses of chloral and bromide by rectum, and slept with one-half hour's intermission for twenty-nine hours, and awoke with good appetite and digestion. This was the thirtieth attack.

She was taken out of school, given tonics and gymnastics, and remained well for eight months, when I lost track of her.

The dominant symptom of the malady is vomiting coming on spontaneously, with no exciting cause. Some of my cases were feverish, one having a temperature of 104°. Holt says the lack of fever is a point of much diagnostic value—a statement at variance with my experience.

The vomiting crises are not due to acute indigestion, gastritis, or bad feeding. The integrity of the gastrointestinal functions is generally perfect, save for the recurring illnesses. No known plan of dietetics will prevent the attacks. Stomach digestion and intestinal peristalsis are temporarily arrested, and are rapidly restored when the gastric irritability is over. Fatigue, excitement, anxiety, school work are more likely to cause an attack than indulgence at the table. Sea-air, country life, no study, are more likely to lessen the severity and frequency of the attacks than semistarvation and

medication. Nevertheless, the condition is apt to disappear in adolescence.

I would state my opinion that the cause of recurrent vomiting is still unknown, but it is probably a transitory autointoxication, playing with full force on the nervous centres governing gastric secretion and motion, that in some cases the lesion of the stomach is an intermittent form of hyperchlorhydria.

DIAGNOSIS. In any suspicious case the urine should always be examined for albumin and casts, and the odor of the breath and the reaction of the stomach contents noted. The first attack will be taken for indigestion, but the course of the malady and recurrence will clear up the diagnosis. Some cases have been mistaken for meningitis on account of headache, vomiting, constipation, and boat-shaped abdomen, but a patient with meningitis does not vomit pure gastric juice or recover in four or five days.

The patient might give an impression of appendicitis or intussusception, but there is no abdominal tenderness, or tumor, or prolapsed bowel, or blood in the stools. A severe attack will cause the physician the deepest apprehension, as day after day he views the rapid emaciation, great cardiac weakness due to loss of fluids, lack of nourishment, frequent retching and vomiting.

Nearly all cases get well, yet as our knowledge of the course of the disease becomes complete, and its relative frequency becomes evident, an increasing number of fatalities are reported. The post-mortem findings are necrotic changes in the gastric and intestinal mucosa and inflammatory or irritative lesions of the kidney. Yet in the most desperate emergency, when the child is apparently moribund, a sudden recovery is probable. Further, any attack may be the last. Some unknown influence may so invigorate the child's vitality that the gastric crises do not recur.

THERAPY. It is difficult to estimate the effect of treatment in an affection that may terminate spontaneously at any time, and in which long periods of health occur. The alkaline treatment was strikingly effective in at least one of my cases, and should always be tried. In dangerous conditions nutrient enemata, chloral by rectum, and hypodermics of morphine and strychnine may tide you over a dangerous crisis.

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MEDICAL TREATMENT OF GASTRIC ULCER.

By Samuel W. Lambert, M.D.,
of New York.

Ulcer of the stomach has always existed and physicians have always treated it, but an accurate knowledge of its pathology and a rational understanding of its treatment date back less than a hundred years. There is probably a medical treatment of gastric ulcer as old as Hippocrates, and it is customary to credit the Father of Medicine with a knowledge of this disease. It is true that he described a *morbus niger* characterized by black vomit, melæna, darkened skin, pain after eating, and loss of flesh and strength, and that he prescribed a diet of milk, sweet and fatty foods, abstention from wine, salt, and spices, further advising bloodletting and mild cathartics, with avoidance of exercise and exposure to the heat of the sun. But such a description and such alleviative measures apply equally well to certain cases of cancer, or of hepatic cirrhosis, or to other causes of gastric hemorrhage, and it seems doubtful if ulcer of the stomach was known as a distinct disease before the last half of the eighteenth century. At all events, it was the epoch-making publications of Cruveilhier in the 30's which placed this disease on the firm modern basis of pathology, and first gave an opportunity for a scientific therapeusis, which Cruveilhier was also the first to formulate.

The indications for such a treatment depend on the general and local conditions present in those afflicted with the disease. The patient is usually anæmic and, because of partial starvation, below the normal standard of nutrition. In certain cases he is a sufferer from severe nervous symptoms. The stomach, in addition to the ulcer, is the seat of a grave functional disturbance, as is evidenced by hyperacidity, with more or less stagnation of food, and by irritability, with vomiting, nausea, and pain. A serious or even fatal complication in the form of a hemorrhage or a perforation of the ulcer is a possibility and constant menace to the life of the patient. But the principal fact to be remembered in treating ulcer of the stomach is that there is no specific and that the ulcer heals through the power of repair in the body. The therapeutic indications may be formulated thus:

I. To assist nature in the process of repair.

a. By regulating the diet.

1. To protect the ulcer from mechanical injury and consequent further extension of the ulceration.
2. To keep the ulcer at rest.

b. By administration of drugs.
1. To stimulate cicatrization.
2. To cover and protect the ulcer from chemical irritation.
3. To neutralize the gastric acidity whether due to the normal acid or to any of the abnormal acids of fermentation.

c. By improving the general health by careful feeding and hygiene.

II. To prevent loss of flesh and strength by feeding through other channels than the stomach.

III. To combat individual symptoms and complications as they arise.

The two cardinal points in every ulcer cure and regimen are rest and milk diet. The oldest treatment consisted of the regulation of the diet, and dates back to Cruveilhier, who advocated, in 1838, a diet of milk exclusively, to be given in small amounts and at frequent intervals, and milk still remains the best food in these cases. But rest is, perhaps, the more important of the two, and was first proposed in the 50's by Brinton, of London, who made it a feature of the treatment which was formulated by him. But the final adoption of rest as an essential in all ulcer cures is due to the careful presentation of this subject by Leube in the 70's and to the influence of von Ziemssen, which was exerted in a publication made about the same time. All such patients should be put to bed and kept there for such a period that the characteristic pain and tenderness consequent upon the taking of a mild but varied diet shall no longer appear. This means that a sufficient period must elapse to allow the patient to pass through the various stages of stomach starvation, milk diet, fluid diet of broths and milk, diet of fluids, eggs, bread, butter, cereals, and lighter meats. The rest cure for cases of gastric ulcer does not mean such an absolute isolation as is indicated for the more serious forms of neurasthenia. It is sufficient that these patients stay in bed and give up all business cares and worries. They may see their friends and the members of their family in frequent short visits; they may be entertained by reading and games, and they may receive letters and even write short replies. During the "rest" they should receive daily alcohol spongings and baths, and mild forms of massage to the arms, legs, and back will improve their general condition. The duration of this rest cure will rarely be prolonged beyond six weeks.

In addition to this general rest a local rest for the stomach and the ulcer itself is indicated, and this brings one to the second cardinal point: the regulation of the diet. As soon as the "cure" is begun and the patient is settled in bed, a period of absolute abstention from food by the stomach should be inaugurated. Nothing but

water and pieces of ice should be swallowed. The feeling of hunger caused by the stomach starvation becomes blunted within a couple of days, but thirst is very troublesome and water must be allowed. Both the loss of nourishment and the loss of fluid may be supplied in some measure by nutrient and saline enemata, although these are poor substitutes and cannot be continued indefinitely. The first week of such treatment is a severe tax on the patience and the confidence of the patient, but some period of starvation by the stomach seems wise, and even in the milder cases the cure will be more certain because of it.

Nutrient enemata were used in the treatment of gastric ulcer by Brinton in conjunction with his rest cure. They are undoubtedly a great assistance in keeping up the strength of the patient. The method of using is to give the patient daily, in the morning, a high lavage of the colon, say of four quarts of normal saline solution. After a rest of at least an hour the regular nutrient enemata may be begun, and may be continued at intervals of four hours during the day. Three, or at most four, such enemata may be given during the twenty-four hours. Each enema should not exceed four ounces in bulk, and may consist of egg, milk, or meat-broths, or of combinations of these foods. All the foods so used should be predigested to a degree of complete peptonization by means of pancreatic extracts and bicarbonate of soda. There is a widespread habit in practice to use this peptonizing process only for milk, and to add to it only the preparations of meat-peptones which are on the market. The freshly prepared peptonized broths and eggs are as easily made as is peptonized milk, and leave no uncertainty as to the amount given. One avoids also the use of alcohol, which is a prominent ingredient of most proprietary peptone foods. Alcohol is not a necessary part of nutrient enemata, and should not be added except for some special therapeutic reason. If the enemata are not well borne, or if the rectum becomes irritable from frequent use, some preparation of opium may be added, and with this assistance the rectal feeding may be continued longer than might be possible without it.

It will be found if the water returned from the morning lavage be measured that a considerable quantity has been absorbed; this will vary somewhat, but it often amounts to half a pint. Such an absorption tends to diminish thirst and to lessen the amount of water demanded by the stomach. It is wise to make further use of this manner of supplying water to the system, and to inject into the bowel a half-pint of saline each evening an hour or so after the last nutrient enema has been given, with the idea that the whole amount will be absorbed. During the night the rectal feeding should be omitted, the patient be allowed to sleep, and the day's routine as outlined be resumed in the morning.

Gastric feeding may be resumed in mild cases within four days,

but in the severer forms of the disease it will be necessary to wait a full week or more. One should begin before the rectum grows intolerant, and should increase the use of the stomach gradually, while the use of enemata is discontinued in like manner. The first food to be given should be peptonized milk in small doses, at rather long intervals. The amount may be increased and the interval shortened until, by the end of a week, the patient will be getting a quart of peptonized milk during the twenty-four hours, and the rectal feeding may be stopped. The progress of the return to a normal diet should be a steady advance from this point on, with some daily change in order that the patient may feel that each day brings an improvement. About two weeks will be consumed in reaching this stage of the cure. The next four weeks will be spent in taking the patient through all the stages of diet which are characteristic of the feeding of infants during the first two years of life, and much benefit can be gained for patients with gastric ulcer from a study of the principles of infant feeding. The main point to be observed in increasing the diet is to make a single change at a time, no matter how simple, in order that if any distress or set-back follows, the new article of diet or the new method of administration may be ascribed as its probable cause. In this manner it is possible to correct quickly any indiscretion in diet and to prevent serious relapses in the course of treatment. But the success of the whole cure depends more on the first step, the inauguration of a milk diet, than on any other detail of the treatment. The use of milk as an exclusive food is subject to much prejudice from the laity and to some misconception even from the profession. I believe it is possible to secure a milk which can be taken by anyone, and would insist on two main propositions: First, there is no method of furnishing a quickly prepared, palatable peptonized milk, but the peptonized milk which is required for use in a cure for gastric ulcer, whether it will be used in the colon or in the stomach, requires the constant application of moderate heat for two hours for its preparation, and the product has a disagreeably bitter, unappetizing taste. Second, the modification of milk, by the dilution of top milk or cream, can furnish a milk of any desired composition. Milk can be so modified that low percentages of casein can be combined with normal or high percentages of sugar and butter fats. And such modified milks, either raw or peptonized, can be made to agree with any stomach, however peculiar the idiosyncrasy of the patient may be.

The popular modification of milk by mixing it with lime-water or Vichy water gives a clue to a method which has been most successfully used with children. It is not so much the addition of the alkali, though that is a help to modify the curd formation, as it is the mere dilution, which is the essential part. Cows' milk has an average constitution of fat 4 per cent., sugar 4 per cent.,

casein 4 per cent., and its casein has the peculiarity of curdling in large lumps. This last peculiarity is usually considered the cause of the failure of the milk to agree, but the abundance of the curd is an equally important factor in causing milk indigestion and gastric irritation. Simple dilution of the milk removes the cause of the trouble, and the use of an alkali as a diluent tends to modify the size of the curd, but there is a loss by the same process in nutritive value by a like dilution of both the butter-fats and the milk-sugar. It will be found that stomachs which are the seat of ulcer will often bear fats well, and although cane-sugar is at times a source of acid fermentation, it is found that milk-sugar is usually well borne. The problem to secure a milk which will not irritate is, therefore, the same as that which has been solved for the artificial feeding of infants, namely, to diminish the proteid and still keep the sugar and fat percentages the same as in normal cows' milk. So much has been written on this subject of late years that it would be superfluous to go farther into detail. It is useless to leave the modification of the milk to the undirected efforts of the average attendant, trained or untrained, but a definite milk formula should be selected and modified as often as necessary. Another source of error can be found in the widespread fallacy that there is a rapid method of peptonizing milk, the so-called "cold process" of proprietary advertisements. It seems absurd that it is necessary to deny the possibility of peptonizing milk by such a method.

After the patient has reached the point where he is on an exclusive stomach diet of peptonized milk, the first advance is to increase the milk till he is taking two quarts or more a day. The next step will be to reduce the degree of peptonization. During the third week the peptonizing process should be cut down to half an hour or twenty minutes' duration, and by the end of the fourth week the milk can be given raw, though modified in strength if originally necessary. During the third week, also, cooked cereal gruels may be added to the milk as part of the diluent. Barley, wheat, and oat flour may be used to advantage in this way. The fourth week will see added to the dietary crust-free bread, butter and boiled egg. One may add during the fifth week potatoes (baked or boiled), rice, boiled macaroni, custards, chicken, and sweetbreads. The final or sixth week of the cure the diet should be increased to include beef, mutton, green vegetables, light salad without vinegar, cooked fruits, and simple puddings. The patient will be allowed out of bed in the fifth week and even earlier in the mild cases. He should be encouraged to exert himself more and more each day, with the hope that he may resume his regular mode of life, except for certain precautions which are essential to avoid a relapse.

The disease tends to recur in new situations as well as relapse in the old, and the rules for a prophylactic diet and mode of life for these cured patients are most important, and their observance

must be insisted on for a long time. Such a patient must avoid frequent eating and drinking, and he must not overdistend the stomach with an excessive amount of food at any meal. He must eat slowly and masticate the food thoroughly. All hard food, like bread-crusts and fruit-seeds, and tough vegetables or meat-fibres, must be omitted in order that there may be no mechanical injury to the gastric mucous membrane. Alcohol in all its forms, spiced and highly cooked sauces and condiments, and even an excess of common salt are to be avoided in order that there may be no excessive chemical irritation of the stomach. Even after the patient has returned to work he must avoid overfatigue, both physical and nervous, and he should abstain from long journeys where he cannot control his diet and mode of daily life.

A specific action in the cure of gastric ulcer has been attributed to certain alkalies and astringents and to two drugs of widely different qualities, namely, the subnitrate of bismuth and olive oil. The alkalies would seem to have no more than antacid and possible laxative action, unless, perhaps, the insoluble calcium carbonate which has been suggested as a substitute for bismuth. The principal astringents which have been used are the perchloride of iron and the nitrate of silver. Both these drugs have a similar degree of astringent action by which the granulating surface will be stimulated to cicatrize, but the silver seems to have given the best results. The nitrate of silver solution must be introduced with a tube in order to reach the stomach in an active condition before it is precipitated as an inert chloride. This alleged disadvantage of the silver salt would seem to be a distinct advantage, not that the nitrate becomes inert, but that by doing so it renders inert a certain amount of the hydrochloric acid of the stomach juices.

The use of bismuth in the treatment of gastric ulcer was suggested in the 60's by Budd and Trousseau, but the definitive claim for a specific bismuth cure has been put forward particularly by Fleiner. Fleiner's mode of procedure is as follows: To wash out the fasting stomach each morning until the water returns clear and is free from an acid reaction, and then to introduce through the tube six ounces of water, with which 2½ to 5 drachms of subnitrate of bismuth have been thoroughly mixed. As soon as the tube is withdrawn the patient should lie down and rest quietly in such a position that the bismuth will gravitate toward the supposed site of the ulcer. After half an hour's rest the patient should be given his breakfast. The result of such a treatment given daily should be immediately apparent in a diminution of the stomach distress and cessation of the pain, nausea, and vomiting. The time to begin the use of the bismuth is coincident with the return of gastric feeding after the initial period of starvation is ended, and should be continued for at least two weeks. Fleiner does not claim that the rest and the regulation of the diet can be omitted;

on the contrary, he states particularly that the bismuth is an aid to the regularly accepted routine as already detailed. Fleiner does claim for the bismuth cure, however, both an antiseptic and astringent action, as well as a direct action to reduce the hyperacidity in addition to the mechanical protective effect of the large doses. Ewald, in the first edition of his *Klinik*, suggested the substitution of the insoluble carbonate of lime for bismuth, and Pariser has recently reported the use of a chalk, talcum, and magnesium mixture in place of bismuth, and with excellent results. The opponents of the bismuth cure have insisted on the disadvantages of its constipating effects, of its discoloring the stools, causing a possible oversight of slight melæna attacks due to small hemorrhages, and of the dangers of using the stomach tube in all ulcer cases. So far as the use of the tube is concerned, it is not an essential, for the bismuth mixtures can be given by the mouth direct, and it has been so given by Fleiner and others, but the other criticisms are not without their significance and weight.

The olive oil cure of Cohnheim is applied in the same manner as is the bismuth cure. The oil is introduced through the tube into the fasting stomach after a moderate lavage, before breakfast, in quantities of from two to four ounces, or it is given before the three principal meals without the use of the tube in doses of from one to two ounces. Cohnheim claims that the oil forms a protective coating to the ulcer, relieves the pain and vomiting and the tendency to pyloric spasm, allows the patient to be fed, and itself acts as a food, and finally that it checks the secretion of acid. His reports would prove that the milder cases can be treated under this oil regimen by simply adding a regulated diet and without any attempt at a rest cure.

Both of these drugs may be given direct by mouth, and have been so used by their adherents, but they require the use of the stomach tube to apply them to the best advantage. This will raise an immediate opposition on the part of many clinicians who have a decided reluctance to introduce a tube into a stomach known to be the seat of an ulcer. It is a difficult task to decide what degree of danger attends such a procedure. If ordinary precautions are taken not to distend the stomach, and not to get too great a pressure by limiting the height of the funnel to the level of the head of the patient, one can ignore the possibility of a perforation of an ulcer. The likelihood of causing a hemorrhage is quite another question. It is doubtful if every clinician has not at some time washed bright blood out of a stomach as a result of the straining and retching due to the irritation of his siphon tube. Such accidents are regularly slight and of no consequence, but at least two authorities have recorded fatal hemorrhage which they believed to be due solely to a gastric lavage. It would seem wise to try the gastric lavage in any case where it was desired to give the patient the

benefit of a thorough bismuth or oil cure, and only to desist upon the occurrence of bleeding as a consequence of the treatment. Of course, cases which have been bleeding spontaneously in the recent past would also be excluded from such procedure.

The treatment of special symptoms and complications forms an interesting and important chapter in the history of this disease. The local subjective symptoms of nausea, vomiting, epigastric distress and pain, are best treated by the treatment of the ulcer itself. They usually disappear during the starvation period which should inaugurate every cure. When they return during the course of the treatment they are to be considered as danger signals that the treatment has progressed too rapidly and that that individual case must be set back to an earlier period of the cure. Nevertheless, these symptoms may require other remedies for their relief than the bismuth, silver, oil, etc., which have been discussed. Antiemetics will often prove of benefit, and anodynes, as codeine, cocaine, and anæsthesin will often control attacks of gastralgia, while morphine should be avoided because it tends to increase acidity. The regular habit of these patients, especially those who have a condition of hyperacidity, is constipation. The most efficient drugs to combat this condition are the alkaline salines, prominent among which Carlsbad water and salts must be mentioned. Such an aperient given each morning before breakfast is usually sufficient. If there be any serious accumulation in the colon, it may be relieved by the use of oil or water enemata. The conditions of thirst and of hunger which are largely due to the treatment itself have been discussed before. The condition of anæmia will require general treatment, and iron will be needed. One can use the pyrophosphate with considerable confidence of having no irritating effect. It may be used during the rest-cure treatment as soon as the patient has begun to add other articles of food to his milk diet.

The most constant accompanying gastric complication is an hyperacidity. This may be overcome in a purely symptomatic way by neutralizing the acid, or the more permanent method of modifying its formation may be adopted. The secretion of the acid may be checked and in large measure controlled by the use of atropin or belladonna. The same result may be secured by the use of bismuth, of oil, and of fatty foods generally, or by irrigations of silver nitrate, as has been already described. The adherents of the oil cure of Cohnheim claim that this simple treatment will overcome most cases of pyloric spasm, even when associated with tetany. Such a procedure demands a trial for no other reason than for its simplicity alone. Two other complications are purely surgical in their treatment: the late complication of gastric ulcer, a cicatricial pyloric stenosis, with its consequent motor insufficiency, and a perforation of the stomach, with peritonitis. Surgery can cure the first, and it is a modern triumph that some degree of suc-

cess is offered in the second, in which form of perforative peritonitis von Ziemssen thirty years ago could only advise as complete an euthanasia as possible.

There remains to be considered the treatment of hemorrhage from the site of an ulcer. This complication may present itself in different degrees of severity. The mildest cases of bleeding in which the amount of blood lost is insignificant may be considered as mere incidents in the course of a disease which is running along smoothly. After any loss of blood which amounts to more than the merest shreds or stains in mucus, discoverable perhaps only by careful chemical analysis of the stools, it is wise to take precautions to avoid irritating food for a day or so. If the blood can be measured by the ounce, a period of fasting should be insisted on as an initial therapeutic measure. This complication is often the first symptom to make these patients realize the severity of their disease, and the therapeutic measures of rest, starvation by stomach, and rectal feeding are frequently begun shortly after a more or less severe attack of hæmatemesis. If the hemorrhage is not repeated, even if it amounted to a pint or more, the regular routine treatment may proceed without a setback. The hemorrhage may become continuous, or it may be repeated at short intervals in spite of treatment, and may demand surgical interference within a few hours. The bleeding may occur at longer intervals, and possibly be associated with each attempt to begin gastric feeding. Such cases present the most difficult question for decision, whether to call on the surgeon for help or to continue medical treatment. A single large hemorrhage, causing death in a few minutes, is also a possibility, and such a complication is, of course, beyond either medical or surgical help.

The medical treatment of active gastric hemorrhage is simple, but often inefficient, and is directed to giving the blood an opportunity to coagulate, and thus to plug the bleeding point. Absolute rest, local application of ice to epigastrium, and the giving of pieces of ice to be swallowed whole, are of some benefit. The stomach should be allowed to contract, and if it be filled with clots a stomach tube should be inserted and the organ emptied. There is only one drug which is of service: the hypodermic use of morphine controls the restlessness and air hunger, keeps the patient quiet, and supports the heart action. The use of alcoholic stimulants is contraindicated, and cardiac whips are decidedly injurious. The loss of fluid and the consequent thirst may be overcome by means of saline enemata. A pint of normal saline solution may be injected into the rectum at hourly intervals, with a fair prospect of its complete absorption, and such enemata may be repeated with advantage for ten or more consecutive hours. A due appreciation of the probabilities of the success of surgery in these cases of hemorrhage, and the utter helplessness of medicine, and of surgery also, unless

the case is undertaken early, will change the medical habits and improve the surgical results of the past.

During the past ten years there have been 52 cases of gastric ulcer admitted to the wards of the New York Hospital. Of these 35 were treated in the medical and 17 in the surgical wards. Of the 52 cases, four were relapses in cases previously treated, so that there were fifty-two admissions of forty-eight persons. Of the 52 cases, eleven died, which is a mortality of 21.15 per cent. in all cases.

Of the 35 cases in the medical wards 30 had hæmatemesis, two of whom died; three abandoned treatment in from two to four days, and were discharged unimproved, and the remaining two were cases of relapse occurring without hemorrhage. The details of the 4 cases of relapse are as follows:

Case I. was operated on for general peritonitis caused by a perforated gastric ulcer in November, 1895, and was treated in the medical division for a relapse without hæmatemesis in October, 1896.

Case II. was cured by operation for a general peritonitis, due to a perforated gastric ulcer, in February, 1898, and was treated in the medical wards for a recurrence without hemorrhage in October, 1898.

Case III. was discharged improved from the medical wards after thirty-nine days' treatment in February, 1902, and died in the surgical service after an operation of gastroenterostomy to relieve a cicatricial pyloric stenosis, in September, 1902.

Case IV. was discharged improved after thirty days' treatment in the medical division in October, 1897, and returned for treatment in March, 1899, but left dissatisfied four days after admission.

Of the 17 cases admitted, or transferred to the surgical division, 3 were admitted moribund, suffering from a general perforative peritonitis, and all died without interference. The 14 cases operated on should be classified as follows: 1 case died after an operation to relieve a cicatricial stenosis, as stated above; 2 cases were operated on for "gastralgia," and in both healed ulcers only were found; both were discharged cured; 3 cases were operated on for hemorrhage, and of these 2 recovered and 1 died; and finally, 8 cases of peritonitis due to a perforated ulcer of the stomach were operated on, with a mortality of 50 per cent.—4 cases recovered and 4 died. The statistical facts of these few cases do not allow of any particular generalization except to emphatically point out the fact that surgical procedure offers in certain cases the only road to recovery.

THE SURGICAL TREATMENT OF GASTRIC ULCER.*

By Joseph A. Blake. M.D.,
of New York.

There is probably no region of the body at the present day in which there is more surgical interest than the stomach. The recent progress in gastric surgery is largely due to the magnificent work of von Mikulicz, Mayo Robson, Moynihan, and Mayo. These surgeons have had the advantage of attracting and controlling very large amounts of clinical material from which to select their cases. Consequently we have from them many observations upon the treatment of cases which ordinarily do not go to the surgeon, and we have had to, and still, look to them chiefly for advances in the surgical treatment of gastric conditions in general. To make my point more clear it is only necessary to reflect that the surgical treatment of gastric ulcer has been hitherto almost entirely directed to its more serious complications, namely, perforation and cicatricial contraction with its resultant obstructions. It is only in the last few years that hemorrhage from ulcer has been treated, to any extent, surgically, and at the present time we are just beginning to recognize what surgery can do for the chronic ulcer which may give no symptoms beyond slight disturbances of motor sufficiency and indigestion, with occasional exacerbations attended by pain and possible hemorrhage. It is in the latter class of cases that we must look for progress both in diagnosis and treatment, for these cases may proceed to perforation and stenosis for which we know there is no remedy other than surgical intervention. Few surgeons other than those mentioned can report series of operations for ordinary chronic ulcer. For instance, my personal experience includes no such cases but only cases of perforation, pyloric stenosis, or hour-glass contraction and hemorrhage. My hospital service is one of the largest and most active in New York, and the utter absence of cases of ordinary chronic ulcer must be due either to a hesitancy on the part of the general practitioner in that city to resort to surgical measures or to a lack of knowledge as to what surgery can do for such cases.

The treatment of acute gastric ulcer is essentially medical, yet, as has been pointed out by Mayo and others, the exacerbations of a chronic ulcer are probably not infrequently mistaken for an acute ulcer, and the cure is consequently not permanent.

Having stated the aspect of the subject in general, it is my purpose to take up the surgical treatment of the phases of gastric ulcer,

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namely, perforation, cicatricial contraction, and obstruction, hemorrhage, and chronic gastric ulcer, *per se*.

PERFORATION. Unless operated upon, 98 per cent. of cases of perforation die. In 1895 Gould[1] was able to collect only 7 cases that had been successfully operated upon. In 1896 Weir and Foote[2] collected 78 cases, with 29 per cent. of recoveries. In this series the mortality among the cases operated upon within twelve hours after the perforation was 39 per cent., between twelve and twenty-four hours 76 per cent. over twenty-four hours 87 per cent.

Since that time the number of operated cases has gone up into the hundreds, with but little change in the mortality other than the betterment produced by the natural improvement in the treatment of peritonitis caused by perforation.

Although advances in general in the treatment of peritonitis have reduced the mortality, the most important advance has been the establishment of the fact that early operation is absolutely necessary for the attainment of good results. To wait for the shock to disappear is simply to invite failure. The shock of a perforation is caused by irritation of the peritoneum, and disappears with the administration of the anæsthetic. Abundant investigations have shown that the contents of the stomach and duodenum are practically sterile, particularly when hyperacidity is present. In a short time, however, the presence of the foreign material in the peritoneal cavity invokes a violent septic peritonitis.

I have not so far lost a case of gastric or duodenal perforation that has come to me within twenty hours of the perforation. In nearly all of these I have washed out quantities of gastric and duodenal contents which had been scattered throughout the entire cavity, and have closed the peritoneum without drainage.

Advance in the treatment of these cases must be in the line of early diagnosis. The diagnosis of a perforative lesion in the upper part of the abdomen is not so difficult; when once seen the picture can hardly be forgotten. If there is a history of antecedent gastric trouble the diagnosis is simpler; but it must be remembered that ulcers outside of the motor area of the stomach may give no symptoms before perforation. A slow or chronic perforation, as it is termed by Moynihan, often gives rise to a local peritonitis and abscess, and the diagnosis may consequently be obscure; yet in these cases there is not the demand for early interference that pertains to acute perforations.

My personal experience with perforated gastric and duodenal ulcers is limited to 6 cases. Two were in women, the ages being twenty and twenty-one years. In both the ulcer was situated on the anterior surface, one at its middle, the other one-and-one-half inches from the cardia. In one the perforation had existed for six days, in the other twenty-one hours. In both, adhesions had formed which had subsequently ruptured, deluging the cavity

with gastric contents and pus. Both died: one on the tenth day, the other on the sixteenth day after operation, from sepsis from subphrenic abscesses. Abundant drainage was employed in both cases.

The remaining cases were males. One of these, a man of thirty-five years, was operated upon forty-eight hours after the perforation, and had a general peritonitis. The ulcer was situated just to the left of the pyloric ring. Death occurred on the fifth day from persistence of peritonitis. The remaining three cases recovered. One, a man forty-seven years of age, was operated upon eight hours after perforation. The ulcer was situated at the pylorus and could not be closed by inversion; it was therefore excised, the incision being planned so that a more or less typical pyloroplasty was done. The foreign material was flushed out and the abdomen was closed without drainage. Convalescence was uninterrupted. He now, one and one-half years since the operation, has some symptoms of motor insufficiency, and I have recommended gastroenterostomy. Another case was operated upon six hours after perforation. The ulcer was also situated at the pylorus, which was stenotic. The abdomen was full of gastric contents and bile. The perforation was one-eighth of an inch in diameter and was closed by inversion, thus also closing the pylorus. The abdomen was then flushed out and a posterior gastroenterostomy performed. The wound was closed without peritoneal drainage. Recovery was rapid. The last case was a man twenty-five years of age, with a small perforation of the duodenum close to the pyloric ring, of forty-eight hours' duration. There was a well-established general peritonitis, with marked distention. A diagnosis of appendicitis was made, with a corresponding incision. Afterward a median incision was made, the perforation found and closed, the ileum opened and emptied to permit of reduction of the intestines that had escaped, and again closed; the abdomen thoroughly flushed and drained by a stab wound below the right ribs and by a drain in the pelvis through the first incision. Recovery was somewhat slow but complete.

Recovery in the cases in this series operated upon within twelve hours was rapid and exceedingly satisfactory. The same has been true of a number of traumatic perforations of the stomach and upper intestinal tract that I have operated upon.

Cicatricial Contractions and Obstruction. Obstruction from cicatricial contraction occurs most often at the pylorus, more rarely at other portions, where it gives rise to hour-glass contraction. Lesser grades of interference with motility are caused by perigastric adhesions or even by the mere presence of ulcers without obstruction in the pyloric portion, and will be referred to later in connection with chronic ulcer.

Pyloric and hour-glass obstructions can be helped only by surgical intervention, which gives most excellent results, the mor-

tality in these cases, unless the patient is nearly moribund from inanition, being extremely low, in the neighborhood of 5 per cent.

While in the cases of uncomplicated pyloric obstruction, Finney's operation has been productive of excellent results, in stenosis due to ulcer gastroenterostomy, with or without pylorectomy, appears to be the operation of choice. Apropos of gastroenterostomy, I venture to report one of my cases of hour-glass stomach somewhat fully, since nature had already elected a posterior gastroenterostomy as a solution of the difficulty. In this patient, a woman twenty-six years of age, I found a typical hour-glass stomach, the constriction being at its middle. On turning up the colon I found what was apparently a congenital deficiency in the transverse mesocolon through which a loop of the ileum had passed and become adherent to the posterior wall of the stomach at the site of the contraction. In liberating this loop it became apparent that the ulcer had penetrated through the coats of the stomach and partially through those of the small intestine. In closing the aperture in the stomach I was able to enlarge the constriction and then perform a gastrojejunostomy with the cardiac pouch. This patient has entirely recovered her health and has no gastric symptoms.

Hemorrhage. Hemorrhage from gastric ulcer is a serious complication. Savariand[3] places the mortality at 66 per cent. In regard to the surgical treatment there are many differences in opinion. The statistics gathered from the reports of isolated cases are also misleading. These variations are traceable primarily to the numerous phases of hemorrhage occurring from ulcer or, perhaps, to put it better, to the varieties of ulcers which happen to bleed.

We owe to Moynihan[4] the most succinct exposition of the subject of hemorrhage from ulcer. His division of the cases is dependent upon whether the hemorrhage occurs from an acute or chronic ulcer. Hemorrhage from an acute ulcer, although frequently violent and depleting, displays a marked tendency to subsidence under medical treatment. This explains the dictum of other observers, Leube,[5] Hartmann,[6] Lund,[7] and others, that operations should not be done for single large hemorrhages. On the other hand, hemorrhage from a chronic ulcer is usually repeated. The hemorrhages may be frequent and small, resulting only in a persistent anæmia, or they may be large and recur at long intervals, or be rapidly repeated. Again, we may find that the hemorrhage may come from one or many small superficial erosions or from one or several typical chronic ulcers.

These variations in the origin of the hemorrhage constitute therefore the differences in the indications for surgical intervention and in the technique to be employed.

My personal experience has been limited to 5 cases operated upon for hemorrhage, with two deaths. Both the fatal cases had

chronic ulcer from which there were several rapidly repeated large hemorrhages. In one the percentage of hæmoglobin was 35 per cent. before operation, in the other 33 per cent. In the first case the ulcer, which was at the middle of the anterior surface of the stomach, was excised, no gastroenterostomy being done. In the second case gastroenterostomy alone was performed. The first case died on the sixth day from what I considered meddlesome treatment in the shape of large repeated infusions, by which the percentage of hæmoglobin was reduced to below 20. The second case died from an extension of the thrombus in the bleeding vessel back into the hepatic artery. In this case the ulcer was situated in the middle of the lesser curvature and had been practically latent. In one of the three cases that recovered a very small round ulcer was excised from the middle of the posterior wall, no gastroenterostomy being done; in the other two, gastroenterostomy alone was performed, the ulcer not being located. These cases had had several fair-sized interval hemorrhages, but were in excellent condition. There has been no recurrence of hemorrhages since the operations. In two of them, however, only three months has elapsed.

My opinion is, that a single large hemorrhage, without previous symptoms referable to ulcer, should not be operated upon, but when there have been antecedent symptoms, operation should be at once performed. In no case should the patient be allowed to drift into a condition of profound anæmia from successive hemorrhages. Also, that cases suffering from recurrent hemorrhages, whether small or large, should be operated upon.

In regard to the nature of the operation I believe that excision of the ulcer combined with gastroenterostomy is the method of choice. Excision, however, is out of the question in profound anæmia and when the ulcers or points of hemorrhage are multiple. It should be done, if practicable, when the ulcer is not in the pyloric portion. Ulcers in the pyloric portion are probably much more amenable to gastroenterostomy alone than when situated elsewhere. Moynihan is a firm believer in the efficacy of gastroenterostomy alone.

Chronic Gastric Ulcer. As already mentioned, the treatment of acute gastric ulcer is essentially medical, since in these cases the results are extremely good. The story in chronic ulcer is different. Russell's[8] statistics derived from a large number of outpatients are that 42.6 per cent. recovered; but of these 27.7 per cent. had had only one attack, and should therefore be classed as acute ulcers, thus leaving only 14.9 per cent. which recovered after having more than one attack. The remaining cases, excepting those that died, were all suffering from gastric symptoms of more or less severity. The average of the figures given by von Mikulicz,[9] Mayo Robson,[10] and others who have collected statistics is not far from

25 per cent. mortality if the deaths from tuberculosis, etc., to which these patients are predisposed, are not included. With these the figures approach 50 per cent. In 1897 von Mikulicz,[9] in a series of 238 operated cases from the clinics of Billroth, Czerny, and himself, found the mortality to be 16.1 per cent. In 1900 Mayo Robson,[10] in 188 collected cases of operations for all complications (excluding perforation and hemorrhage), found the mortality to be 16.4 per cent.; yet in 1901 he reports the mortality of his own cases to be only 5 per cent. Moynihan[4] reports 88 similar cases with a mortality of less than 5 per cent. The Mayos'[11] statistics up to April 1, 1904, in 328 operations for the improvement of gastric drainage, some of which were performed for malignant diseases, are as follows: 20 pyloroplasties, no deaths, but seven secondary operations; 40 Finney gastroduodenostomies, one death; 271 gastrojejunostomies, with a mortality of 6 per cent. in the benign cases. In the very few cases which I have operated upon for benign pyloric or other obstructions I have had no deaths.

It may be well to consider the reasons, other than a distinctly lesser mortality, why surgical treatment has the advantage. Besides the elimination through excision of the tendency to malignant degeneration, which occurs in 6 per cent. of the cases, there are still other points. In the first place it is a question whether the hyperchlorhydria which often accompanies ulcer is not a result instead of a cause of the ulcer. Soupault[14] reports complete relief from hyperchlorhydria and gastrosuccorrhœa in several cases in which pylorectomy was done for ulcer at the pylorus. Pylorospasm, which is frequently caused by the presence of an ulcer, at once yields to excision or gastroenterostomy.

The majority of symptoms causing ulcers are situated in the pyloric portion and are consequently at a point where the utmost benefits are derived from gastroenterostomy. On the other hand, let us for a moment view the matter from the opposite standpoint and consider the dangers of gastroenterostomy. The operative procedure to one who is accustomed to it is very simple and is followed by very little discomfort or shock. I am always surprised at the slight reaction following the operation, it being usually much less than that following the interval operation for appendicitis. The relief, if pyloric obstruction has been present, is immediate, and is evidenced by the general expression of the patient even on the day following the operation.

The vicious circle, owing to better methods, is no longer to be feared. It was due apparently to the employment of a long loop of intestine in either the anterior or posterior operation with a too high implantation in the stomach. It has been combated by an enteroenterostomy, by the Roux method, by a lower implantation, and, finally, by eliminating the loop and using the very commencement of the jejunum where it naturally lies in relation with

the posterior wall of the stomach, as in the Petersen operation. I have found that this method gives excellent results.

Peptic ulcers in the jejunum sometimes follow gastroenterostomy. Mikulicz,[12] in a study of 15 cases, finds that they are not dependent upon a hyperchlorhydria as is usually supposed, but that they may occur when the percentage of hydrochloric acid is below normal. He also finds that they occur only after anterior gastroenterostomy. This may be explained by the fact that a much longer loop of jejunum is necessary in the anterior operation and that consequently the mucous membrane is less protected by the bile.

The danger of contraction of the anastomotic opening is largely preventable by a proper technique which eliminates the production of excessive scar tissue.

Many ask, "Why does gastroenterostomy cure gastric ulcer?" The explanation of its curative action upon ulcers situated in the pyloric portion is simple. This part of the stomach is very muscular, and its chief function is to force the partially digested food through the pylorus. Consequently an ulcer situated there is constantly subjected to traumatism, not only by the contractions of the stomach, but also by the passage of food across it. This trauma is accentuated if there is any obstruction, organic or spasmodic, at the pyloric opening. A proper drainage opening situated to the left of the pyloric portion at the most dependent part of the stomach affords complete rest to the pyloric portion and at the same time drains away any excess of gastric secretion.

Its beneficial action upon ulcers in the cardiac portion is not so clear, but here, also, the more rapid emptying of food and secretions must produce some result. If possible, however, it seems to me that excision of ulcers in the cardia should be practised.

But besides the institution of drainage there is a further field for surgery in the liberation of adhesions, the plication of dilated stomachs, and in fixation.

Viewing the results surgery has accomplished in these cases, one must concede that the treatment of gastric ulcer should be, at least, largely surgical. Our plea is for earlier resort to surgical measures; not only in ulcer but in malignant disease. By the time the diagnosis is evident by chemical or physical aids the patient is often beyond relief. As Munro[13] puts it, surgical treatment should be instituted "not late but early; not as a last resort, but before the starvation, the long suffering from pain, dyspepsia, and fermentation absorption have reduced the patient until he is beyond surgical help; before he is anæmic from persistent bleeding or peritonitic from culpable delay."

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A CASE OF GENERAL MILIARY TUBERCULOSIS, WITH AN OPEN FORAMEN OVALE AS A FACTOR IN ITS PRODUCTION.

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The role of a persistent foramen ovale in permitting pieces of thrombi and tumor cells to pass directly from the right auricle to the left side of the heart has been brought into prominence by various investigators. In none of the literature consulted is there mention of the passage of bacteria through such an opening in the interauricular wall. It is our opinion that we have a case in which tubercle bacilli were disseminated through the avenue of an open foramen ovale. Other interesting features of the case now to be described are the extent and size of the tuberculous nodules on the peritoneum and the tuberculous invasion of the pancreas. Though aware of the hypothetical nature of the conclusion regarding the pathogenesis, I feel, from the data, that the inference is highly probable and of great interest in relation to general miliary tuberculosis. Throughout the work I have had the assistance and helpful criticisms of Dr. A. P. Ohlmacher, the director of the pathological laboratory of the Ohio Hospital for Epileptics.

Clinical History. Only the following points have been obtainable: C. E., aged twenty-four years, was a male, colored, an imbecile, and an inmate of the Ohio Hospital for Epileptics for ten years. He had had idiopathic epilepsy for thirteen years. His grand mal attacks occurred principally at night and at irregular periods. His family and previous history were unobtainable, except that until the day before his death he was up and about and that within the last two months of his life he had failed visibly in weight and strength. His physician was called one evening for the reason that during an attack the patient had bitten his tongue severely, almost severing the organ about an inch from the tip. Examina-

tion revealed a startling prostration, a temperature of 101°, a weak, irregular pulse of 127, and a respiratory rate of 40 per minute. That the tongue wound could cause the observed signs was not deemed possible, but before enough data could be collected for a diagnosis the patient died. The lethal ending was not attended with status epilepticus nor with any single grand mal attacks.

Gross and Microscopic Morbid Anatomy. The body was fairly well nourished. The anterior inch of the tongue was almost entirely separated from the rest by a deep, gangrenous wound. The oral cavity was otherwise normal. Subcutaneous lymph nodes, except the inguinal, were not palpable, and the latter showed no unusual size. The testicles were of equal size, small, and soft, and presented no nodules to the touch. There was no fluid in the abdominal cavity. The parietal peritoneum adhered to the omentum. The intestines were matted together. All these adhesions could be broken without much difficulty. Both surfaces of the abdominal serosa were studded with an immense number of large, yellowish, confluent, elevated nodules, which were somewhat hard and recalled to mind tumor metastases. The liver and spleen were likewise somewhat firmly bound by the peritoneal exudate to the diaphragm, to the parietal peritoneum, and to the neighboring viscera. The pancreas was practically embedded in the exudate and in a cordon of large glands. The mesenteric lymph nodes were only slightly enlarged. The iliac, the lumbar, the aortic, and especially the cœliac glands were much increased in volume. The anterior and posterior mediastinal glands were much above normal size. There were adhesions in each pleural cavity over the entire lung, which connections were easily broken by the hand. There was no fluid in either pleural sac.

The heart and pericardium together weighed 425 grams. The latter was adherent to the heart all over. On stripping off the pericardium some yellowish nodules were seen. The cardiac orifices and valves were normal. There was a slight hypertrophy of the left ventricle. The musculature of the right auricle was thickened and its endocardium was cloudy and dense. The foramen ovale was open, and a diagonal slit, admitting a one-quarter inch probe and running anteroposteriorly from left to right, made communication between the two auricles. The fossa ovalis was deep and bulged to the left. The ring of Vieussen was well developed and protruding, and was continuous with a thick, pronounced Eustachian valve. Microscopic examination revealed fresh tubercles in the thin exudate on the epicardium. The musculature showed a recent myocarditis, but no tubercles after a search through many sections.

The right lung weighed 930 grams, the left 800 grams. They were similar, of a deep-red color, and crepitated somewhat. The pleura was slightly thickened. Cut surface showed a pale brownish

color and numberless whitish tubercles of the size of millet-seeds, which were likewise plainly seen when the pleura was stripped off. Both lungs were searched for old caseated foci, but none was found. At the apices the tubercles were somewhat larger to the eye than in the rest of the lung, a fact which is of interest in view of Hansemann's[1] recent contention that in simple miliary tuberculosis there is no difference; but there were no old lesions, like cavities, fibrous changes, or calcareous deposits. The bronchial glands were large, but were discrete and not soft. Microscopic examination of the lung itself showed many tubercles of small size, in the largest of which there was some breaking down in the centre, but practically all of them were discrete. The lymphoid and epithelioid elements of the tubercles were distinct, but it is noteworthy that giant cells were found in only very few of them. Other characteristics of the lung sections were a moderate dilatation of blood-vessels and many alveoli and bronchi filled with cells, a mucoid substance, and considerable detritus—in short, some of the evidences of bronchopneumonia.

The spleen weighed 440 grams, and was adherent to the diaphragm, the liver, the stomach, and the intestines. At the hilus of the organ there were four or five somewhat enlarged lymph glands. The spleen was large and firm, and, on the capsule, there were numerous large, yellowish, elevated nodules, similar to those on the other peritoneal surfaces. It cut readily and the brown pulp showed no increase of connective tissue but a great abundance of whitish, pinpoint spots universally diffused. Microscopically it was somewhat difficult to differentiate the miliary tubercles at first glance, inasmuch as there were no giant cells present and the Malpighian bodies were numerous. However, on closer study, the epithelioid cell centre and ring of lymphoid cells served to distinguish the tubercles from the Malpighian bodies with their uniform structure of lymphoid cells and the accompanying arteriole. Only here and there were tubercles showing a central degeneration.

The liver weighed 1840 grams, and was bound firmly to a mass formed by the pancreas, the stomach, neighboring parts of the large and small intestines, and some large lymph glands near the cœliac axis, one of which was almost as large as a hen's egg and situated a little to the left of the hilus of the liver, closely associated with the portal vessels. The gall-bladder was in the mass, and one could not say whether the ducts were patent or not, for, owing to these adhesions, the bile could not be squeezed out nor could the ducts be probed. There were no gallstones in the gall-bladder or ducts. The liver was large and firm. There were nodules on its capsule similar to those on the spleen. The organ cut readily and the incised surface showed many whitish tubercles of pinpoint to pinhead size. The markings of the liver were indistinct and there was no congestion. Besides its involvement with

the structures in the mass above mentioned, the liver was adherent to the diaphragm, to the spleen, and to the right kidney. In stained sections the liver showed a great number of fresh tubercles; in fact there were more in the liver in any microscopic field than in the lungs. Here, again, it was noted that only a few presented well-formed giant cells, although in the liver sections the greatest number was found. The tubercles were all of approximately the same structure, with practically no central caseation. On the whole the age of the tubercles, judged from their microscopic appearances, must have been about the same in the liver as in the lungs and spleen. The hepatic parenchyma was otherwise about normal. The intercellular connective tissue was prominent, but there was nothing approaching a cirrhosis. There was no abnormal distention of the vascular system.

The left kidney weighed 165 grams. It was large and waxy looking. The capsule stripped with ease and did not tear the parenchyma. The decapsulated surface showed only a slight injection and a few whitish, circumscribed tubercles, some of which were seen on cut section. The cortex was somewhat increased in thickness. The right kidney weighed 150 grams and was similar to its fellow except that on cut section tubercles could be made out more distinctly. Microscopically a few fresh tubercles were seen in the cortex and in the medulla of both kidneys. Here none was found with the typical giant cells of tubercle, although in one there was a large cell with several nuclei. Otherwise the following conditions were found: (*a*) glomerular tufts were much distended; Bowman's capsules were unchanged, but between the tuft and the capsule there was a good deal of detritus, with an occasional cell; (*b*) the epithelium of the renal tubules was cloudy and desquamated; (*c*) considerable vascular dilatation; (*d*) connective tissue was not increased—briefly the changes of an acute diffuse nephritis. Sections were treated for the amyloid reaction, with a negative result.

Both suprarenal capsules were small and hard, but showed no nodules or caseation. Microscopically, besides the usual fatty infiltration, there was noted a pronounced hyperæmia, especially toward the medulla. There was no degeneration of cells. After examining a considerable number of sections, two tubercles were found, one fresh and one with a partial central degeneration, and neither showing a giant cell.

The pancreas weighed 120 grams, and, as mentioned before, was surrounded by enlarged tuberculous glands, and directly upon its head lay the largest of the cœliac glands. Microscopically there was no increase of connective tissue, the gland tubules were unchanged, and the islands of Langerhans were intact and of usual size. One partly caseated tubercle was found in the parenchyma in the lower border and just at the edge. It was entirely within the pancreas, though its outer lymphoid ring extended to the

extreme edge of the lower border of the organ. A more prolonged search would probably have demonstrated other tubercles.

The prostate was soft and not enlarged, and microscopic examination disclosed no trace of tuberculosis or other inflammation. The testicles were, by an oversight, not saved, but palpation had revealed no nodules or enlargements of any kind, and both vasa deferentia were, at autopsy, found regular and of their usual consistency.

The peritoneum, as indicated before, exhibited a most striking hyperplastic tuberculosis. The nodules were as large as a bean in many locations, and the whole process was diffuse and confluent. The tumor-like nodules reminded one a good deal of the "Perlsucht" of cattle, and compared favorably with the description of a form of latent tuberculosis of the peritoneum given by Kaufmann.[2] Sections of such nodules showed an extensive caseation, only the periphery containing tissue not degenerated. There were no ulcers in the intestines, which were negative except for a slight increase in lymphoid tissue.

All of the abdominal and thoracic lymph glands presented a great augmentation in size, but a gradual decrease in size of the glands from the abdomen up was noticeable. The largest ones were the lumbar and cœliac. Those in the mediastinum were about the same volume as the bronchial glands. The deep cervical nodes were slightly larger than normal. Unfortunately, nothing further can be said of the inguinal glands except that through the skin they showed no marked increase in size. Microscopically these all revealed an advanced caseation. Those in the cervical region were similarly destroyed, but in them the process could be denoted comparatively recent, for there were many fresh, well-developed tubercles present.

There was a persistent thymus, with imperfectly developed corpuscles of Hassal, but no tuberculosis of that organ was found, though it lay within a mass of tuberculous glands. The thyroid was negative.

The brain weighed 1235 grams. The dura was unchanged. The pia was slightly cloudy over the convexity. Otherwise the encephalon was negative except that there were a few slender adhesions between pia and dura at the base in the region of the circle of Willis and under the frontal lobes. No tubercles could be definitely made out, and, in spite of the basal adhesions, sections of the pia in those regions contained no evidence of tuberculosis. The spinal cord was negative.

Direct smears from the peritoneum and liver showed no acid-resisting bacilli. In those from the lungs and spleen only a few such bacteria were found. Blood-serum inoculations from the spleen, heart's blood, peritoneum, and pia remained sterile. From the lung staphylococcus aureus and albus were isolated. From the liver there was obtained a short, thick bacillus, which reacted

in all ways like the colon bacillus, and was probably an artificial contamination.

COMMENTS. In summing up and interpreting the foregoing data, I wish to prove three things: first, that the primary seat of the affection was in the abdominal cavity; second, that the general tuberculosis originated by the lymphogenous route; third, that the open foramen ovale was instrumental in the production of the generalized disease.

It is of prime importance to take some position regarding the original seat of the inflammation. The tuberculosis of the lungs, the liver, the spleen, the kidneys, the suprarenals, the pancreas, and the pericardium was of recent origin, while that of the thoracic and abdominal lymph glands and of the peritoneum was, judging from the size of the nodules and from the extent of the caseation, much older. For these reasons, I assume, and I believe with justification, that the tuberculosis began in the abdomen, and there, no doubt, in the peritoneum, inasmuch as such an affection is not uncommonly primary in the serous covering.

Taking this for granted, under our second heading, the chain of lymph glands from the iliacs up demands some consideration. The lymph nodes around the iliac vessels were considerably larger than usual, the lumbar were still larger, and the cœliac glands were most extreme in size. This increase in volume corresponds with the areas drained by, and with the tributaries of, the groups mentioned. Following up through the thoracic cavity the mediastinal glands were all enlarged, about the size of those in the lumbar region. This chain of glands, I believe, was the path by which the tuberculous material travelled from the peritoneum to the thoracic duct and thence to the heart. This is one of the acknowledged paths for the production of a general miliary tuberculosis, it making no essential difference, as far as result is concerned, whether the tuberculous material breaks through the walls of the thoracic duct or arrives there from its tributaries. This route, first demonstrated by Ponfick, is found especially in tuberculosis of the glands of the abdomen.[3] The thoracic duct was not discoverable in the mass of tuberculous tissue, but the fact that we did not find it is of no importance, for, from the anatomical relations of that vessel to the general glandular system, it was destined to transmit the infectious material.

The possibility of a miliary tuberculosis, consequent to the invasion of a pulmonary bloodvessel, was carefully excluded. Beginning with the arterial and venous trunks, all of the bloodvessels of the lungs down to the smaller ones were carefully slit open in search for a thrombus, an embolus, or an eroded vessel. The result of this dissection was entirely negative. To put this conclusion beyond criticism, sections were cut from the areas where the bronchial glands lay nearest the intima. This examination removed any

possible doubt. Nowhere did the tuberculous process approach nearer than the adventitia of the vessel, and, in the majority of cases, a dense connective-tissue ring interposed between the outer coat of the vessel and the degenerative process.

Finally, it is necessary to support our third contention. Having arrived at the right side of the heart, there are possible, because of the presence of the open foramen, two distinct means of dissemination of the tuberculous material. One is by way of the pulmonary artery to the lungs and then back to the left heart and thus to the general circulation, constituting a condition of secondary emboli. Against the assumption that this was the exclusive path, the appended arguments could be brought: (*a*) The lungs in our case do not show any greater invasion than the liver or spleen, which they would have done under the above hypothesis, for tuberculosis is pre-eminently an embolic process.[4] That conditions for embolism and thrombosis are present in capillaries only a few hours after tubercle bacilli arrive in them has been shown recently by Wechsberg[5] and by Miller.[6] All of the organs involved in the acute distribution of the bacilli in our case showed tubercles of about the same age, and though some of the bacteria could undoubtedly escape the lungs and get to the systemic circulation, as careful microscopic work would show, there would not be present, under those conditions, the uniform number of tubercles of the same structure as were found in the lungs, liver, and spleen. (*b*) There would not be present such auspicious conditions in the heart, the details of which have been enumerated and will be further described. (*c*) Such a pulmonary route would probably not be the one in a rapid development of the disease as occurred in our case, evidenced by the lack of giant cells, as indicated by Birch-Hirschfeld,[7] and by the nature of the history of the case. (*d*) Such a path is operative in all cases where tubercle bacilli pass through the pulmonary artery to the lungs, causing miliary tuberculosis there, and yet a systemic invasion of equal grade in all organs is not shown in such instances. The literature has been searched in vain for some specific statement upon the question, not which organs are affected in hæmatogenous miliary tuberculosis when the embolic material passes first to the lungs from the right heart, but whether the intensity and age of the process in the several organs are equal. The table given by Eichhorst[4] (p. 614) and the ones quoted by Birch-Hirschfeld[7] (p. 351) are not to the point. Recently, however, some experiments have been performed by de Haan[8] which give an answer to this question. Assuming, with probability, that there was no open foramen ovale in either of two animals inoculated by de Haan, and to be mentioned here, the conditions of these experiments are just those that I am now discussing and am trying to show to be inadequate to have caused the general miliary tuberculosis of our case. De Haan inoculated tubercle bacilli into the

left jugular vein of a horse and of a Javanese beef. At the end of seven weeks, because of great prostration, the horse was killed. The autopsy showed the liver, the spleen, the pericardial sac, and the abdominal cavity to be normal. There were a few tubercles in the kidneys. The lungs, however, were so invaded by tubercles that there was present almost no air-containing tissue. The other animal was killed at the end of nine weeks. It had been affected with the distoma, and the liver presented a corresponding change, but no tuberculosis of that organ is mentioned. The lungs were much involved with miliary tubercles, but the other organs were normal. To the argument that a single introduction of tubercle bacilli invalidates these results for our purpose, it may be stated that in the experiment with the horse a cheesy thrombus remained at the sight of inoculation, which was always a source of further infection. An added proof, the value of which may be questioned, is the work of Strauss and Gamaleia,[9] who injected intravenously a culture of dead tubercle bacilli and found miliary tuberculosis of the lungs, but none of the spleen or liver. (*e*) It appears, from anatomical relations and from the hyperplastic nature of tuberculosis, that the infectious material must get directly into the aortic side to cause a widespread miliary disease and of equal magnitude. Because of all these enumerated facts and arguments, I feel confident that the general miliary tuberculosis of our case was not produced by way of the pulmonary artery. For the sake of completeness, it might be mentioned that a very improbable explanation of the miliary disease under discussion is by retrograde lymph flow to the organs from the glands into which they drain. It is highly probable that the cervical and, no doubt, the inguinal glands were invaded this way from the thoracic nodes. The age of the process in the former glands is too extreme to have been produced by the route that caused the tuberculosis of the other organs.

The other method of spread and the only other avenue open is by way of the patent foramen ovale. The conditions in our case are exactly those that Rostan[10] and Zahn,[11] who have thoroughly discussed the subject of embolism through an open foramen ovale, call the essentials: a thickened endocardium and an increase in the thickness of the musculature of the right auricle; a well-developed Eustachian valve; thickened and protruding borders of the fossa ovalis; a bulging to the left of the base of the fossa; and an open foramen, which in our specimen admits a quarter-inch probe. The cause that will produce an increase of pressure in the right auricle, so imperatively demanded before there will be a passage through the foramen, was certainly present as a bronchitis, and later as a bronchopneumonia at the first onslaught upon the lungs by the bacilli by way of the pulmonary artery. Rostan says that the bulging of the valve of the opening is a positive proof of

such an augmentation of pressure, and Zahn states that, besides this bulging of the fossa to the left, the best anatomical proofs in the right heart of the presence of a stasis and an increase of pressure are the hypertrophy of the muscular walls, the enlargement of the fossa, and the thickening of its edges. Therefore, we have all the requisites for the passage of blood and foreign material from the right auricle to the left, and, though the tuberculosis of the lungs was in large part produced by way of the pulmonary artery, it is highly probable, with such a direct path open, that the production of the general miliary tuberculosis occurred in largest part by way of the open foramen ovale to the aortic side. With the large percentage of such persistent openings in the interauricular wall that is found at autopsy (v. Rostan and Zahn, *loc. cit.*), it is surprising that this route has not been dwelt upon before.

The tuberculosis of the pancreas in our case is of interest only because of its apparent rarity. Most writers dismiss the subject with the statement that it is not often seen. According to some authors, when such a condition is found it exists in a lymph gland on the surface or embedded within the pancreas. Kundrewetzky,[12] however, in 128 cases of consecutive tuberculosis, found 12 positive tuberculous affections of the pancreas, or 9.37 per cent.; in 18 cases of general miliary tuberculosis he found this organ invaded six times, or 33.3 per cent. In children he found 44.44 per cent.

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A BICEPHALOUS MONSTER.

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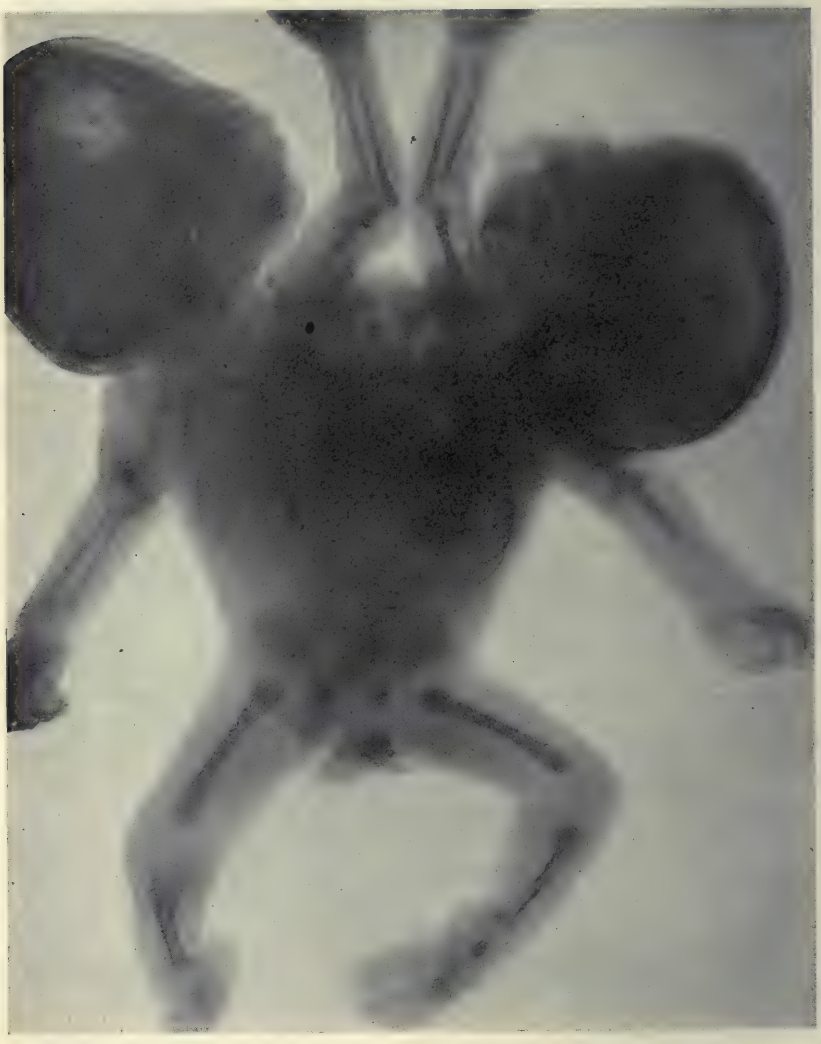
On March 21, 1904, a young woman was admitted to the hospital in labor at term. Nothing unusual was observed on inspection of the contour of the abdomen save that it was probably slightly more conical than usual. The pains were strong and normal in every way, occurring at intervals of about three minutes. On vaginal examination an apparently normal L. O. A. presentation was diagnosed; membranes intact and well down on the pelvic floor. These were ruptured, and the scalp speedily appeared at the vulvar opening. The delivery of the head was more tedious than was expected, retraction after each pain being very marked. It was finally accomplished, however, but rotation did not follow, nor could the child be drawn down. After a short interval the head turned rather rapidly toward the left, rotating about 90 degrees. Here it stopped, and the child seemed absolutely immovable. Efforts at traction were unavailing. Examination showed the shoulders blocking up the pelvic outlet and tightly wedged. Under full anæsthesia, by manipulation and traction, the arms were freed and brought down, though both humeri were broken in the procedure. The child now began to breathe, but the rest of the body seemed as immovable as ever. Suddenly a third hand appeared outside the vulva. After about half an hour's hard work there was a second sudden rotation, still to the left, of 90 degrees, and the child was easily drawn away, the second and right head being turned over on the anterior aspect of the thorax facing the left. The cord was tied, and a rather small placenta delivered without difficulty. Bleeding was very free from the cervix, which showed a bilateral laceration, and was immediately closed by sutures. There was no external laceration.

The monster after birth began to breathe through both mouths, and lived for about two hours, cardiac pulsations growing gradually weaker. When examined the child presented a perfect specimen of a bicephalous monstrosity, with two heads, four arms and shoulders, and a single trunk. At birth the weight was nine and one-half pounds, and the measurements were as follows:

	Left head.	Right head.
Circumference	33 c.m.	33⅙ c.m.
Diameter of heads:		
Bitemporal	7 "	7 "
Biparietal	8 "	8½ "
Occipitofrontal	11½ "	10 "
Occipitomental	12 "	12½ "
Suboccipitobregmatic	12 "	13 "

Circumference of thorax	46 c.m.
Diameter of thorax, sagittal	7 "
Parietal	20 "

The fusion anteriorly seemed to be complete below what normally would have been the junction of the manubrium and gladiolus, while posteriorly there were two distinct vertebral columns, the inner set of ribs fusing by cartilaginous bands. The pelvic girdle consisted of five distinct bones—two normal external ilia,



joined anteriorly in a normal symphysis; two normal sacra, each with an attached coccyx, and a wedge-shaped bone uniting the sacra and evidently representing the fusion of the internal ilia. The details of the bony skeleton are well shown in the accompanying skiagram prepared by Dr. S. H. Heller.

After the death of the monster a partial autopsy was made, care being taken not to injure it more than absolutely necessary. The abdominal cavity was opened, and the contents appeared nearly normal. The anus was imperforate, and the rectum enormously distended with meconium. There was a single stomach, into which two œsophagi entered in the median line through practically a common opening. The liver was large, and apparently from its irregular shape represented the fusion of two organs, there being, however, but a single gall-bladder. The kidneys were normal, the testicles undescended. On examining the thorax two hearts were found in a single pericardial sac, while the lungs showed two apparently normal external lobes, while the internal lobes were more or less fused.

The mother of the child was of German extraction, belonging to one of the numerous religious sects which make up the farming population of Lancaster county. She was eighteen years of age, unmarried, and had been delivered late in March, 1903, of her first child. She was the oldest of a large family, and nothing abnormal could be ascertained in her family history. The father was a light mulatto, and the child showed unmistakable evidence of negro blood. The mother's convalescence was uneventful.

TWO CASES OF VIOLENT BUT TRANSITORY MYOKYMIA AND MYOTONIA APPARENTLY DUE TO EXCESSIVE HOT WEATHER.

By David L. Edsall, M.D.,
of Philadelphia.

Localized acute muscle cramps, especially in the calves, are not uncommon and are sometimes very severe; but, excluding tetanus and other conditions due to poisons or to distinct lesions of the nervous system, widespread cramps are rare, and, as acute conditions, they are seen chiefly in connection with profuse diarrhœa (cholera and cholera nostras) or tetany; and even in these conditions the spasm does not usually involve the trunk muscles. Furthermore, true tetany is seldom and cholera almost never met with in this country.

In the cases that I am about to describe there was exceedingly violent tonic spasm, involving all the extremities as well as the abdominal muscles; the characteristics of tetany were not present; there was no noteworthy digestive disturbance; and the tonic spasms occurred as interruptions of a most remarkable grade of myokymia. The whole disturbance subsided with extreme rapidity,

and in both cases was apparently due to exposure to excessive heat. The myokymia was an even more peculiar and striking feature of the cases than the tonic spasm. Very high grades of fibrillary contraction are, at best, rare, when unassociated with demonstrable organic disease; and I cannot determine that myokymia of such brief duration as that in my cases, but, at the same time, of a comparable degree of severity, has heretofore been described.

In their chief symptoms my cases resembled, on the one hand, the frequently quoted cases of Talma, which he thought presented conditions so far resembling those in Thomsen's disease as to deserve the name of myotonia acquisita; and, on the other hand, the cases of Kny and Schultze, in which there was a remarkable grade of myokymia without noteworthy tonic spasm. As Schultze remarks, the chief feature in his case was the severe fibrillary contractions; while in Talma's the chief feature was tonic intention spasm; in my cases, however, both these features were present and were very severe; and the most remarkable fact concerning them was their brief duration.

Besides the brevity of the attacks, their relation to heat is of interest. In the cases of Kny and Schultze, and in two of Talma's, the conditions present were referred to exposure to wet and cold; and others have made similar observations. The frequency of muscular cramps in swimmers, too, is a matter of tradition. I think that slight degrees of localized cramp to which the subjects pay but little attention, and which occur particularly in the calves, are not uncommon during excessively hot weather, even when digestive disturbance is absent; but I do not know that exposure to excessive heat is recognized as a cause of myospasm. The literature on sunstroke and heat exhaustion, at any rate, contains, so far as I can determine, no reference to such a complication or sequel.

In this relation it is interesting that one of my patients was so subject to cramps when bathing that he had been unable to learn to swim; and, on the other hand, that before the severe attack during which I saw him he had repeatedly had mild attacks of cramps in the extremities when overheated, and when no digestive disturbance was present. Evidently there was in this case, as shown by the history of the patient's childhood, a persistent tendency to myospasm; and, with this predisposition, extremes of either heat or cold tended to cause more or less severe myospasm, his attack while under my observation having been a great exaggeration of the more common conditions.

Although this man was admitted after the other, I shall describe his case first, for I did not see the other patient during his most acute symptoms.

Case I.—J. H. P., aged thirty-one years, a locomotive fireman, was admitted to the Episcopal Hospital July 3, 1903. His family history was entirely without bearing upon his condition; of his

immediate family, he had lost one brother, of an unknown cause. He had had measles and scarlet fever during early childhood, and pneumonia at the age of nine years, and was said to have had walking typhoid fever later. He had malaria three years ago, having had this disease also when a child. He is subject to brief attacks of diarrhœa, which he thinks are largely due to drinking ice-water. During the last year, when overheated, he repeatedly had in his hands and feet cramps somewhat resembling those in the present attack, though very slight in degree. He has also never been able to swim on account of his tendency to these cramps. He states that upon emotional or other excitement he has always had a good deal of twitching in his hands, and that when at school, if told to write upon the blackboard, excitement sometimes increased this twitching to such an extent that he was unable to hold the crayon and would repeatedly drop it. He has also often noticed slight twitching in the calf muscles.

The present attack began on July 2, 1903, at about three o'clock in the afternoon, while the patient was at work on his engine. The weather was very hot; he became greatly overheated, and was suddenly seized with painful cramps, beginning in the fingers, and almost immediately afterward appearing in the calves of the legs, the thighs, the forearms, and the abdomen. These cramps gradually grew worse until the time of his admission to the hospital. For some hours before admission they had been very frequent and exceedingly painful, although the individual spasms were of brief duration. He had had no disturbance of digestion at the beginning of the attack or until about fifteen hours thereafter. He then became somewhat nauseated and vomited once. His bowels had been normal. He had eaten a small piece of salt mackerel on the morning of July 2d; but, except for this, he knew of no possible dietetic cause. He had taken no other sea-food, no fruit, and no milk or ice-cream.

Upon admission, physical examination showed the patient to be a muscular, well-nourished man. His face was flushed, as the result of his occupation and of the slight fever present. His tongue was clean, but rather dry. His abdomen was neither distended nor tympanitic, and there was no abdominal discomfort other than that caused by the frequent spasms in the muscles of the abdominal wall. The lungs were clear throughout, and the heart was negative. The arteries were not at all sclerosed, so far as could be determined. Examination of the liver, the spleen, and other abdominal organs was likewise entirely negative. There was slight enlargement of a few lymph glands in the groin and the axilla, and a few very small cervical glands could be felt.

The most striking feature of the case—and a very remarkable one—was the constant fascicular contraction in the muscles of the feet, legs, thighs, abdomen, hands, and forearms. There were

also occasional slight twitchings of the muscles of the nose and of the rest of the face, and of the upper arm. This movement was by far most pronounced in the muscles of the calf, where it gave rise to continuous pulsatile or wave-like motions beneath the skin, these taking place with the utmost rapidity. Contractions appeared synchronously in various portions of the calf muscles, and continued with such energy and rapidity that they suggested the movements of a mass of very lively snakes. Next to the calf-muscles, the muscles of the forearm and of the hand showed the most active movements. They were, however, much less striking in this region, for while some portion of the affected muscles exhibited fibrillary contractions almost constantly, the individual contractions were much more distinctly appreciable as such than they were in the calves, because only one or two portions of the muscles showed contraction at one time, while in the calves there was a maze of motion. The movements caused frequent twitching of the fingers, somewhat like a mild subsultus tendinum. They produced no movements in the feet or toes. The fibrillary twitchings elsewhere were decidedly less striking and less constant, and the individual contractions were so far separated as to time and space as to be individually quite distinct.

Besides this myokymia, the patient presented very slight persistent carpopedal spasm, most marked in the hands, which were always held in a position somewhat resembling slight tetany; the fingers were slightly flexed at the metacarpophalangeal joint, the thumb being adducted and in apposition. The position was not that of perfectly typical tetany, as the fingers were spread apart somewhat, the first finger in particular being decidedly abducted and occasionally strongly extended. There was a constant feeling of slight stiffness or contracture in the hands, and, except during the more violent spasms, the man was continually rubbing his hands gently in the attempt to relieve this stiffness. The anterior and posterior muscles of the calf, also, were constantly in mild spasm, the foot being held slightly rigid at right angles to the leg. The abdominal muscles, likewise, were practically all the time in very slight contracture.

The mechanical irritability of the muscles was greatly exaggerated. Very gentle palpation caused no spasm and was not painful. Moderately active palpation of the muscles; sudden, moderate pressure, or, even more markedly, a slight tap upon them would bring on violent and exceedingly painful local tonic spasm, during which the muscles would become board-like in hardness. At this time even gentle palpation of the muscles was painful. The spasm would last for fifteen or twenty seconds, and sometimes a little longer, and would then gradually relax, there being a distinct after-contracture, which took about half a minute to disappear.

Even a slight attempt at voluntary use of the muscles of the trunk or the extremities would often bring on violent spasm; and on attempting to sit up in bed the muscles of the abdomen became as hard and firm as a plaster cast, the spasm being exceedingly painful. Any active movement of the hands or the feet would bring on a spasm. I could not determine that there was any entirely spontaneous spasm. At times this seemed to occur, but usually, I think always, it could be referred to an attempt at voluntary movement. Mechanical irritation of the muscles, as by a blow, sometimes caused general spasm of the muscles of the extremities and abdomen; but this, I think, was due to the fact that the pain of the local spasm produced by the blow made the patient unconsciously throw his muscles almost immediately into action elsewhere, thus secondarily bringing on the spasm of these other parts. There was no spasm of the back or neck and no trismus. There was no abnormal mechanical irritability of the nerves; Trousseau's and Chvostek's phenomena were absent, as was Hoffmann's phenomenon.

There was no tenderness over the nerves. Changes in skin sensation were absent, and, except during the painful spasm, there were no subjective disturbances of sensation beyond some numbness of the hands. The knee-jerks and arm-jerks were slightly excited. The plantar reflex was not excited, and the epigastric and cremasteric reflexes were normal. Babinsky's phenomenon was absent.

I had no galvanic battery at hand, but excitability to the faradic current was greatly increased. The weakest current obtainable threw the muscles into violent spasm, just as did mechanical irritation. Tetanus was produced whether both electrodes were applied over the muscles, avoiding the nerves, or one electrode was put over the muscle and the other on the sternum.

The patient's mental condition was entirely normal, except that he displayed the slight soporosity to be expected with his fever. When I saw him his temperature was 101°; upon admission it had been 99.3°. Two or three hours after I saw him his temperature fell, and by the next morning it was normal, rising again that afternoon to 99.4°. Soon afterward it fell to normal and remained so subsequently.

Large doses of bromide were given, and also magnesium sulphate every hour until he was purged. The painful spasms disappeared entirely the evening of admission, and the fibrillary twitching became very much reduced. On the following day the patient was entirely free from painful spasm, and the muscles had quite lost their abnormal irritability to voluntary movement or direct mechanical stimulation. There was still fibrillary twitching in the calves and forearms, but of only slight degree. The urine, examined meanwhile, showed normal conditions, except for a

slight trace of albumin. The blood examination soon after admission showed: hæmoglobin, 93 per cent.; red cells, 5,640,000; leukocytes, 12,200.

The man remained entirely comfortable after this, and on the 6th demanded his discharge. At this time it was noted that his general condition was entirely normal. The tendon reflexes were normal. There was very slight fibrillary twitching in the calves and forearms, but the patient stated that this was usually present. The reactions to the faradic current were the same as were those in a normal man tested at the same time, and there was no abnormal irritability of the muscles.

CASE II.—L. S., colored, of unknown age (about fifty-five years), was admitted on July 1, 1903. I did not see this patient during his active symptoms, but Dr. Despard, at that time my resident, made careful observations and afterward, when the other patient was admitted, stated that the conditions were almost exactly alike in the two cases.

This man gave a negative family history and could not remember any previous disease. He had never had muscular cramps or twitchings. He said that this illness had begun after he had been hard at work and had become much overheated. He was seized with violent cramps in the muscles, first of the hands and then of the arms and legs. The cramps rapidly extended to all the muscles of the body, with the exception of those of the head and face. The attack came on at about eleven o'clock in the morning and he was admitted to the hospital late that afternoon. Meanwhile he had felt nauseated and had finally vomited once, and this had entirely relieved his nausea.

When he came in he exhibited a condition that need not be detailed, as it was practically the counterpart of that in the case already described. Painful spasms that were of brief duration but that occurred frequently affected most violently the muscles of the forearms and hands, and of the calves and feet; but also involved the thighs, the upper arms, and the trunk. Between the spasms there was constant and violent fibrillary twitching of the muscles of the extremities and of the trunk, that in the calf muscles being particularly pronounced and of much the same grade as in the other case. The mechanical irritability of the muscles showed the same excitation as in the other case. The electric excitability, unfortunately, was not tested at this time. Subsequently (when the patient was entirely over his spasms, however), the response to faradism was tested and found to be normal. As in the other case, the spasms were exceedingly painful. The patient showed no other abnormalities, except that there was a very high grade of arteriosclerosis, all the palpable arteries being hard, rough, and tortuous, and the urine showed the conditions to be expected with this —*i. e.*, a trace of albumin and a few hyaline and pale granular casts.

This man was purged, and nothing else was done for him. After having had a free bowel movement he was much improved, and by the following day was practically well—except that he still had a slight tendency to spasms and a very little fibrillary twitching in his muscles. Both the spasm and the twitching disappeared within about twenty-four hours after this. He was not tested during the attack for Chvostek's, Trousseau's, or Hoffmann's phenomena. The day after his admission, when I saw him first, and when he still had slight cramp, the phenomena mentioned were all absent. At that time the condition was so slight that I did not test the response of his nerves and muscles to electricity, doing this only later, when the admission of the other patient and his violent symptoms had made this man's condition of greater interest. The response to faradism was then, as stated, normal.

The cause of the phenomena in these cases is, of course, largely a matter of speculation. The short duration of the symptoms and the rapidity with which they disappeared after practically no treatment but mild purgation suggest a toxic origin. This statement, one that is perhaps somewhat too freely used nowadays when we are in the presence of the unknown, means in this case nothing more definite than that probably the high atmospheric temperature itself, or some little-marked digestive derangement produced by the heat, disturbed the body chemistry in some obscure way; although, on the other hand, I do mean by this suggestion that it seems improbable to me that the heat produced the condition directly, through mere irritation. The general body temperature of the first patient was but slightly elevated, except during a brief period; while the second showed practically no fever: and there are no observations indicating that elevation of the body temperature without toxæmia, even when the fever is very decided, tends of itself to excite spasm. The more or less pronounced spasm not infrequently seen in acute infections is almost certainly due less to the fever than to the toxæmia. There is, then, no good reason to believe that the slight elevation of body temperature exhibited by these patients had any direct relation to the spasm.

It is of couse possible that the immediate effect of the external heat upon the skin may have excited the spasm reflexly, but this seems to me an unsatisfactory explanation; for greater heat than this when applied in the form of hot baths tends to relax such spasm rather than to increase it; and in these patients hot baths had never produced any tendency to spasm. I have, however, already referred to the fact that in the cases of Kny and Schultze, and in two of Talma's exposure to cold or to cold and wet excited the spasm, and I have also noted the effects of cold water in my first case. These observations, and particularly the common con-

ditions in swimmers' cramp, suggest that reflex irritation alone might possibly have excited the spasm.

This question is one that cannot be definitely settled. It is somewhat analogous to the nature of tetany, in connection with which there has been so active a discussion as to the relation of reflex action and toxæmia in the production of the spasm. In tetany the most satisfactory evidence certainly points toward toxæmia; and I think that the same is true of most of the acute and subacute cases of other forms of myospasm.

It is conceivable that the heat itself had nothing directly to do with the myospasm, that both my patients had some digestive disturbance that was but little evidenced by symptoms, and that toxic material absorbed from the digestive tract set up the spasm; but in the absence of anything more than nausea and slight vomiting, especially as these symptoms came on only after severe spasms had lasted several hours, such a source of the toxæmia, while possible, seems to me improbable and at best purely suppositious.

It at first occurred to me that, as they probably are in cholera, for example, the spasms in these cases might have been due to loss of fluid. If, however, this cause was active in my cases, it must have been the result of excessive sweating, as diarrhœa and severe vomiting had not occurred. Since I could not determine that either patient had been sweating excessively, this cause seems very improbable; and the blood count in the first case, although slightly high, is distinctly against such a view.

There is one other factor of sufficient interest to deserve mention, and this is the high degree of arteriosclerosis present in the second case. Walton has laid special stress upon the relation of arteriosclerosis to myospasms, and it is not improbable that in this case it was an important predisposing factor. In the first case there was apparently habitual predisposition; there was certainly no evident arteriosclerosis.

As to the classification of these cases: Any attempt to carry this out definitely is, I think, a somewhat fruitless task, except that it may be stated that they belong to a heterogeneous group, and will not fit well in any place in a schematic classification. The patients showed severe tonic intention spasm and presented at least several features of the myotonic reaction. Following Talma, therefore, and dwelling especially upon the tonic spasm, they might be classed as transitory acquired myotonia. On the other hand, Kny classes his cases as most closely related to paramyoclonus multiplex of Friedreich; and Dana agrees that myokymia is best placed in this class. Talma's name for his cases, however, is hardly justified by any intimate relation to Thomsen's disease, and Dana's view is strongly opposed to that of Gowers and Walton, and it seems to me that the latter authors justly exclude myokymia from the class that includes paramyoclonus multiplex. That my

cases have any serious connection with either Thomsen's disease or paramyoclonus multiplex seems to me to be almost out of the question.

If one is to make a definite classification merely on the basis of certain striking clinical symptoms, these cases might equally well or better be brought into a group with tetany. In a number of points they clearly resembled tetany; but, on the other hand, the tonic spasms were almost entirely intention spasms; the myokymia was quite as marked a feature as the tonic spasm; considering their severity, the attacks were remarkably brief for tetany; and much more important than these facts, the Chvostek, Trousseau, and Hoffmann phenomena were absent. Hence, these cases certainly cannot well be classed with tetany.

The variety of classifications adopted by various authors when dealing with the myospasms shows that the manner in which many of these conditions are grouped is largely a question of personal fancy. This can, it seems to me, scarcely fail to continue to be the case until the nature and the manner of causation of the various myospasms become clearer than they are at present.

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A CASE OF PAPILLOMA OF THE BLADDER, COMPLICATED WITH PYONEPHROSIS, WITH REMARKS ON THE SURGICAL TREATMENT OF PAPILLOMA.[1]

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G. W., aged fifty-seven years, had noticed that for several months his urine had been mixed with blood; but other than a certain amount of weakness following these hemorrhages and a dull pain in the left lumbar region, the patient feels fairly well. Upon questioning, however, he complains of certain vague dyspeptic symptoms and dryness of the mouth. No headache. Sleep is uninterrupted, and examination of the thoracic viscera reveals

[1] Read by title at the meeting of the Urological Association of France, Paris, October, 1904.

nothing abnormal other than a slight chronic bronchitis. Pulse 80, hard, and rather tense. Some general arteriosclerosis. The urine contained a considerable amount of pus, blood, and renal cells from the pelvis of the kidney.

Cystoscopic examination of the bladder showed a body situated on the left side of the bladder wall in the vicinity of the ureteral orifice, but its exact nature could not be made out on account of the clouded condition caused by the presence of blood.

After several days of preparatory treatment of milk diet and the exhibition of urotropin a transversal suprapubic incision was made, and the bladder opened, and by digital exploration a polypus of soft consistency and distinctly pedunculated was found seated in the floor of the bladder to the left of the middle line. In size it might have been that of a large walnut.

The growth was seized as near its base as possible, and its pedicle was excised along with a certain amount of the surrounding vesical mucosa. Sutures were then inserted, and the resulting wound closed without much loss of blood.

On account of the presence of pus in the urine it was decided to drain the bladder. The suprapubic wound was loosely packed with iodoform gauze, and a permanent catheter was inserted.

The after-course of events was simple. The catheter was removed at the end of the sixth day, and the iodoform gauze packing was changed daily until the eighteenth day, when only a small opening remained through which very little urine was voided, the greater proportion being expelled by the urethra. In four weeks' time the suprapubic opening had completely closed, and the patient was discharged.

The patient was seen three months after the operation, complaining of pain in the left lumbar region, recurrence of the hæmaturia, and chills. The temperature was 38.8° C., and the pulse was weak and irregular at 110. The suprapubic incision was found in excellent condition, firm union having taken place.

The urine contains a large amount of blood and pus. Tongue dry, and digestive disturbances, which had somewhat improved before the patient left the hospital, had returned with greater severity than before.

By palpation an enlarged left kidney could be easily detected, and it was thought that fluctuation could be elicited.

The next day the kidney was exposed by a transverse incision and freely incised, which gave exit to about 500 c.c. of dark-red and very ill-smelling pus. Two large drainage tubes were inserted and the wound packed with iodoform gauze.

Within a day or two the temperature had dropped to normal and the pulse to 90, and was of better quality. The patient also commenced to recover his strength, and was able to take a fair amount of food. From this time on the progress toward recovery

went on uninterruptedly, and he was discharged, with a renal fistula, five weeks later.

Eighteen months after the last operation we saw the patient in excellent health, but still discharging a certain amount of urine, and some pus by the fistula from the kidney. But on account of his excellent condition and the absence of all symptoms pointing to uræmic poisoning, we have thought it best to desist from doing a secondary nephrectomy, which can always be resorted to should the indications point that way.

In considering the history of this case it would appear to us that in all probability there was a relationship between the papilloma and the suppurative renal process, inasmuch as the vesical neoplasm probably obstructed the ureter, causing a retention, and the kidney thus weakened easily became a prey to secondary infection.

Microscopic examination of the neoplasm showed the ordinary picture of papilloma without any evidence of malignant transformation.

I would like now to discuss briefly the surgical treatment of papilloma of the bladder in a general way, and, although I have nothing novel to offer, I can at least describe those methods which at my hands have proven the most satisfactory.

Small pedunculated papilloma in the female may occasionally be successfully removed without much difficulty through the dilated urethra; but this manner of operating I believe to be unsurgical, for the simple reason that one is working in the dark, and if the urethra is dilated to the extent requisite for giving a large enough operative field, permanent incontinence of urine is the usual inevitable result, and for this reason I believe that the suprapubic incision is the proper one to select, as I have already pointed out in a paper entitled "Chirurgische Behandlung des erworbenen unwillkürlichen Harnabganges bei Frauen," and published in the *Monatsschrift für Geburtshülfe und Gynäkologie*, Band xix., Heft 4.

Other intravesical operative procedures applied to the male have been described from time to time, such as Chismore's aspiration with a metallic catheter, etc., but all such methods are defective, inasmuch as the operation is performed entirely in the dark. On the other hand, Nitze's cystoscopic technique is certainly a vast improvement over the older manœuvres, and, although this distinguished *confrère* has published thirty-one cases in which he obtained excellent results, it would appear that this ingenious invention has not found many supporters.

The reasons why Nitze's method has not been adopted in general is because the removal of a large papilloma requires a number of sittings, and when one is dealing with a patient already in a weakened condition, the *séances* can only be undertaken at considerable intervals. For most surgeons this is enough to deter them from undertaking the removal of a papilloma by this method, and, on

the other hand, I believe that the majority of patients would prefer to take a little ether and have the neoplasm removed at once and for all than to be continually tampered with.

I would also point out that Nitze himself admits that accidents may occur during or after the execution of these intravesical operations, such as severe hemorrhage or cystitis, irritation of the kidney or its pelvis, as well as febrile disturbances, which simply mean a septic condition; and, last of all, but by no means the least important, prostatitis or epididymitis has been known to supervene. On another occasion Nitze says that severe hemorrhage from the growth, severe cystitis, a small bladder, etc., will render the intravesical operation impossible, and if the neoplasm is of large size, or when there are several growths, the execution of the operation is extremely difficult.

Now, if such an expert as Nitze himself is in these matters admits such difficulties in the operation, it is quite natural that the average operating surgeon will select another technique on which he can rely with practically perfect security. It is evident that many of the present defects in Nitze's method may be removed by the improvement in the instruments, so that the future of this procedure may be increased, but for the present it would appear that its application is extremely limited.

In opposition to intravesical operations we have three techniques by which the tumor may be exposed and removed. The first and oldest of these is Thompson's median perineal incision, which at the present time has lost its diagnostic value on account of the general use of the cystoscope, while its therapeutic importance for the removal of papilloma is practically *nil*, but its applicability for the removal of calculi may be still reserved for certain cases. This procedure may give satisfactory results to a few picked operators, but it is to be doubted whether it will ever be generally employed, because, on the one hand, there is always considerable danger of accidentally wounding the bladder, and, secondly, one never can be sure that he has completely removed the growth. The demands of modern surgery that the field of operation should be freely exposed will certainly place this method in the background, more especially so when one recollects the great possibility of hemorrhage during the operation and the very great difficulty one would meet with in controlling it through the perineal incision.

Koch collected thirty cases operated on by Thompson's method, and in only two was the complet eremoval of the neoplasm a certainty. In five no recurrence had taken place after the first year, while in seven no symptoms returned for two and one-half years; five patients died during the first few weeks following the operation, death being partially due to exhaustion resulting from the severe hemorrhage during the operation, and partly from some intercurrent affection. In more than six of the cases no opinion

could be formulated on account of the short lapse of time since the operation, while in three cases a recurrence took place for the simple reason that the neoplasm was only partially removed. In one case there were three recurrences due to an incomplete removal of the growth. It would seem from these cases that an entire extirpation of the neoplasm is not possible to attain excepting in a few instances unless the tumor grows near the urethral opening of the bladder or in the pars prostatica, under which circumstances König is of the opinion that the perineal incision is more advantageous than the suprapubic opening.

Colpocystotomy for the removal of papilloma in the female bladder has only a limited field of usefulness. The operation is impossible when the vagina is small and also when the tumor grows from the anterior wall of the bladder. Then, again, large-sized growths can only be removed by this route with difficulty, and then only by resorting to morcellation.

Suprapubic cystotomy is in all probability the method now generally employed for the removal of papillomata or other vesical growths. Combined with Trendelenburg's position it fulfils all the requirements for the complete exposure of vesical neoplasms, because a complete view of the entire cavity of the bladder may be obtained, and all parts are accessible to operative manipulations. There is no doubt in my mind that by this route the greatest convenience and security are to be obtained, and as far as hemorrhage is concerned, there is no other technique which gives such absolute security as this one.

The defective points in the operation are, first, the danger of opening the peritoneum, and, secondly, urinary infiltration of the pelvic cellular tissue; but the progress of surgery has practically done away with the first danger, so that should the peritoneum be opened it can be immediately closed, and no ill result is apt to accrue. The dangers of infiltration of urine can be, I believe, easily avoided by proper drainage.

It would also seem to me, from a very large experience, that the transverse suprapubic incision is far more preferable than the median one, and in corpulent patients it certainly gives a far more extensive field of operation.

To render the bladder more ready of access, the injection of air is, to my mind, better than sterile liquid, because, when the latter runs out through the abdominal wound, it inundates the entire field of operation, and if the bladder is infected, the liquid carries the agents of infection with it, which may infect the cellular tissue. Petersen's rectal bag should never be employed, being both useless and dangerous.

The removal of the papilloma, whether pedunculated or not, should include the removal of a certain amount of mucous membrane around the base of the growth, followed by a careful suturing

of the remaining defect. Some surgeons are satisfied by simply ligating the pedicle, cutting off the growth, and then applying the thermocautery to the stump; but this procedure is not safe, because one can never tell whether the growth has commenced to undergo malignant transformation, and in its removal it is more prudent to assume the possibility of malignancy.

Regarding the dangers of purulent infection of the prevesical cellular tissue, I believe with Kraske, that the use of the permanent catheter is not alone sufficient, and that unless the bladder is free from cystitis it is all-important to obtain free drainage. If, however, the urine is apparently aseptic the bladder and the abdominal wound should be closed by a careful suturing, and the bladder drained by the use of the permanent catheter.

To effect a perfect drainage of the wound, the use of iodoform gauze loosely packed in and changed daily is, to my mind, the proper way, and secondary union will follow quickly. The resulting cicatrix is firm, and urinary infiltration is avoided. This manner of drainage is to be recommended in cases of purulent cystitis and, in fact, after all operations where bladder drainage is required for a short time following an operation. Combined with this, the use of a permanent catheter should be resorted to as long as the patient can comfortably bear it and its presence in the urethra gives rise to no untoward symptoms.

SOME UNSETTLED AND IMPORTANT PROBLEMS IN THE TREATMENT OF ACUTE LOBAR PNEUMONIA.[1]

By Beverley Robinson, M.D.,
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To the practitioner of medicine there is no subject of greater interest than the treatment of pneumonia. This interest proceeds from the facts: 1. That pneumonia is met with frequently in all climates and seasons, everywhere, in hospitals, and in private practice. 2. It is a very fatal disease, of rapid course, and of markedly infectious type at times. 3. It has been the subject of a great number of books, papers, discussions from the ablest and most experienced physicians in the past and at the present time. 4. While there is a consensus of good medical judgment as to the efficient cause of pneumonia, as to many accidental and co-operating causes, as to certain indications of treatment, and as to usual causes of death due to it, there still remains much that is undetermined in its treatment, and about which many "good men and true" hold divers opinions.

[1] Read before the American Climatological Association, June 4, 1904.

In my remarks I wish to be understood as limiting the discussion as far as possible to acute lobar or croupous pneumonia, with a consideration solely of the usual dangers or complications occurring in its course.

I would merely add, for additional clearness in the beginning, that certain cases of pseudolobar pneumonia are with difficulty differentiated from the true form, either by symptoms or by physical examination. It is true that the debut of the pseudo form, the temperature chart, the previous bronchitis, the absence of herpes and flushing of the face, the bacteriological findings of several kinds of micro-organisms, and not merely the pneumococcus of Fraenkel, and the isolated areas of consolidation preceding, it may be, and probably recognized before the lobar consolidation is formed, will permit, as a rule, an accurate differentiation to be made. And yet there are cases, as I believe, in which the most careful clinical observer may remain somewhat undetermined as to which form of disease he has to do with for one or more days. Indeed, the autopsy alone has in rare instances definitely solved reasonable doubts.

In this discussion I do not propose to deal with statistics of my own or even of others which I might readily obtain. This has been done already many times, and in the aggregate in a vast number of cases. I regret to say that the resultant figures have not been very encouraging, nor have they shown great progress in treatment; nor have we seen, apparently, the virulency or the mortality of the disease decrease, if we carefully consider the records of a certain period of years in the same or different places. Besides, it must be admitted that statistics as made unfortunately do not tell, never will tell, perhaps, precisely what should be a true and proper estimate of prognosis in any given case of pneumonia. Personality, circumstances, antecedents, temperament, constitutional peculiarities or defects, all differ or are of untold variation. Again, as we all know, epidemics of pneumonia, or the endemic, sporadic sort, show more or less virulence or intensity of poison, depending upon causes, of which we know now, as heretofore, very little in an accurately scientific manner.

Before I speak of problems in curative treatment, let me say a few words in regard to prevention of pneumonia. I do not wish to dwell on facts about which we are all pretty nearly agreed, namely, to avoid excesses, overfatigue, chill, bad air, etc., but upon some which later investigations of others and personal observations render valuable.

We know to-day that the pneumococcus is found in the secretions of the throat and mouth of many healthy people and for long periods of time. One or more of the contributive causal conditions referred to may render these micro-organisms virulent or infective. Is it not specially indicated, therefore, to make use of antiseptic gargles

and mouth-washes frequently when we have reason to fear the possible beginning of pneumonia? This antiseptic mouth-wash, at such times, should have a slightly acid reaction, simply because we know that the pneumococcus does not thrive in an acid medium. Incidentally I should add that, on account of the deleterious action upon the teeth, I do not approve of a mouth-wash of acid reaction to be used habitually in a condition of normal health.

With the first symptoms of chill, fever, pain in the side, cough, and expectoration, I believe beechwood creosote should be vaporized more or less continually in the patient's room. I am confident there is no drug used in this way which has more preventive value in the treatment of pneumonia. Of course, I cannot prove to others that several times already by this means I have prevented in private practice, as I believe, what otherwise would have become pneumonia. Whether it would have become croupous pneumonia or bronchopneumonia, I am not prepared to say except in a hesitating way, and with, it may be, a conviction tending toward the latter opinion. I wish it to be understood that I only give to creosote a very slight or moderate antiseptic power locally; but I know it is an anticatarrhal agent of great value directly and by elimination through the bronchial mucous membrane. Further, I am thoroughly convinced it is the best way to give creosote so as to obtain its constitutional effects without disturbance of the stomach, and, as a rule, without injury to the kidneys. It is wise, of course, if creosote be used freely in inhalations, to examine the urine carefully and frequently for any appreciable amount of albumin. If this be present we should try to determine its cause—whether it be the result of the pneumonia or of the action of the creosote, and act accordingly.

Occasionally, creosote by inhalation used too freely gives headache to the patient or to the nurse. In this case it should be intermitted for a few hours, perhaps, and the room thoroughly ventilated. It is also my belief that creosote thus used prevents the taking of pneumonia by the nurses in attendance or by any near relative very constantly in the room.

The degree of risk of contagion in *the air* is, of course, a questionable matter, and for my part in the majority of instances I doubt the reality of it. In other exceptional instances and in certain epidemics when the pneumococci are more abundant or more virulent, or both, than usual, the transport of the noxa of the disease through the air no doubt occurs, and may be best neutralized primarily by insisting upon having the vapors of creosote in the room. Of course, the sputa should be rigidly and systematically disinfected, and the lips and other parts of the face which have been soiled with them properly cleansed. So, also, must all soiled garments and bedclothes be suitably disinfected upon removal, and after the recovery or death of the patient the furniture and room should be properly

fumigated, cleaned and ventilated, just as we should do in the case of any other possibly virulent contagious and infectious disease. The sputa should never be allowed to become dry, but should be received in a convenient receptacle containing a solution of carbolic acid or bichloride of mercury. If the pneumonia becomes developed I believe antiseptic mouth-washes and creosote inhalations should be continued throughout the acute stage of the disease, and, indeed, until the local consolidations have been resorbed.

The necessity of a large well-ventilated room, with open fireplace if possible, of two well-trained, careful, judicious, and attentive nurses, of proper assimilable food (mainly milk), of a sufficient quantity of good drinking water, and of due attention to the emunctories, namely, the skin, bowels, and kidneys, is all-important, but need scarcely be insisted upon with my audience.

Now we come to some points of judicious curative treatment of pneumonia which are very important, and about which also there may be very different judgments. Among the poor it is difficult, almost impossible, to treat pneumonia as it should be treated, because of the lack of proper surroundings and nursing, not to speak of food, drugs, and very good medical care. Under these circumstances is it proper to transport the patients to the hospital? In general, if the patient be seen at the beginning of the attack, I believe we should do so. Later, at the third, fourth, or fifth day of the disease, to my mind, it is often questionable. Once in the hospital bed such a patient will undoubtedly get better care than at home, and on this account has a better chance of recovery.

On the other hand, when we consider the fatigue, the exposure, the unavoidable nervous upset incident to this change, it becomes a nice question to decide at times, and there is no absolute rule to lay down in advance. The patient and the doctor must decide. If the patient still be reasonable and not too critically ill he may go to the hospital if he desires, and the doctor may consent, if the hospital is not too far removed, an ambulance be had, proper stimulants be given before removal, the patient be thoroughly covered and the removal be conducted in a quiet, expeditious, and thoroughly efficient manner. If the room and surroundings be tolerable and the care of the patient be fair, although not of the best, proper duty to the patient must be decided upon and carried out, after careful and due consideration of everything involved in the individual instance.

When the patient reaches the hospital should he be treated in the general ward? Not so, if it can be otherwise ordered. His chances of recovery are not so good as in a private room or in a small ward where there are only two or three other patients. The noise of the ward is objectionable; the light of the ward is also objectionable. Noise is unavoidable here; light can only be subdued by cutting off air in a measure; inhalations cannot be carried out as

well and as efficiently. I have tried and know of what I speak. So far as other patients are concerned, *pneumonia patients* should be isolated; not because all patients are infective or contagious to others, with proper care and precautions, but a few possibly or probably are, and in time of a prevailing and increasing epidemic influence this should be considered, and more than usual protective care to others should be insisted upon. Of course, I do not wish arbitrarily to ignore the difficulty of doing this, especially if there be numerous pneumonia patients, as has been true during the past winter and even now. Nevertheless, the indications should not be lost sight of. On the contrary, they should be insisted upon, and as far as possible carried out.

A word, now, in regard to the results of treatment in hospitals. Many times it is most unsatisfactory. Again, in certain seasons, we get a series of cases which do well almost invariably, and really with very little active treatment of any kind. In fact, a wise expectancy seems to be most judicious and to afford very good, perhaps the best, results. Why, indeed, should we expect good results from hospital treatment as a rule and when the cases of pneumonia are of a virulent type? They are brought into the hospital usually at a time when the disease is well advanced (second, third, fourth, or fifth day), sometimes almost moribund, and we begin to give our stimulants or other remedies. Already the patient has had, in addition to an acute and virulent disease, imperfectly and perhaps very ignorantly cared for at home for forty-eight hours or more, the *risk* of having gone through all the anxiety, fatigue, exposure, etc., of the transportation to the hospital. Further, we have often to do with poorly nourished and broken-down subjects prior to the attack —subjects, it may be, already of disease of heart or kidneys. Too frequently they are victims of alcoholism or some drug habit. Again, they are of all ages, and the very young and those of advanced years are of the number. Given all these conditions, how may we fairly compare results of treatment thus obtained with what we should obtain, with what we do obtain sometimes, many times, it may be, in private practice?

There is one other thing to which I wish to direct careful attention in this connection, and one far too often overlooked practically in the treatment or estimate of every virulent disease, and particularly when the poison is very intense in quality if not in quantity. *The time of the treatment* when begun is most important—essential and decisive at times in regard to the ultimate outcome of the disease. By doing the right thing at the right time life may be saved; when there is delay in doing the right thing life may be lost. The analogy here which I would refer to is the use of antitoxin in toxic diphtheria. Made use of in the beginning in sufficient doses, the patient will probably recover; delayed in its use, or given in too small amount and not repeated, the patient may die. The patient

will *surely die*, sometimes even with the help of a most wonderful remedy. So I believe it to be in a measure with the treatment of acute lobar pneumonia. Put your patient to bed immediately on the advent of serious symptoms of the disease in a large, sunny, well-ventilated room, provide him immediately with the best nurses and good milk and water; begin immediately antiseptic inhalations, and use all our other curative means sensibly, judiciously, appropriately, and I believe many bad cases may be saved. But delay these primary and efficient, though simple, means too long and the patient will often die. He will die because the poison of the disease has taken hold of him too strongly, in too large quantity, and before proper and suitable means have been employed to check or throttle it.

Now, there are some cases of pneumonia, as there are some cases of diphtheria, enteric fever, scarlatina, smallpox, etc., which will almost inevitably die to-day, as always up to the present time, no matter what treatment is employed. And the proof of it lies in the record of medicine for one hundred years or more. Indeed, the virulency of some of these cases is such as to render them well-nigh hopeless, and they will remain so unless medical science gives us curative sera superior to any we now possess. We must also bear in mind here and ever that we shall have occasionally to do with what occurs both in hospital and private practice, namely, the complications of the primary disease, such as Bright's disease, pericarditis, meningitis. These diseases being present, the case must be managed rationally and in view of everything involved. Despite the best care and treatment, they add much to the gravity of the prognosis, and in some instances they make recovery almost impossible.

One of the most important problems connected with the treatment of pneumonia is the safe and proper use of opium or its alkaloid, morphine. In the beginning, when the pain in the side is intense owing to the complicating pleurisy, it is occasionally indicated to give a hypodermic injection of morphine to allay or arrest suffering. I find little or no objection to the use of the drug in moderate dose at this time, provided the kidneys have not been diseased previously. When the pain is only moderate I prefer local applications as being frequently sufficient to diminish or stop the pain, and because they are useful doubtless in limiting local congestion of the lungs. Later in the disease (and up to the second, third, or fourth day), and despite the judgment of many good observers, notably Dr. Samuel Wilks, of Guy's Hospital, who feels happy only when five grains of Dover's powder are given every four hours in pneumonia, I prefer to abstain from its use except in the rarest instances. I do not believe the opiate has any good effect upon the march of the pneumonic process; I do believe it is prone to lock up secretions which are already too much interfered with by the disease itself. Professor William

T. Gairdner notably has directed attention in the grave and advance forms of pneumonia to the great and immediate danger resulting from the use of an opiate. To dull the respiratory nervous centre at such a time, when nature is striving all she can to protect herself by increased frequency of breathing against inroads of a disease which prevents proper oxygenation of the blood, is to hasten the death of the patient or at least to diminish his chances of recovery. Dr. S. S. Burt has again directed attention to this subject, and in my judgment very wisely. Of course, distinctions should be made. If the patient be of middle life, with previous evidences of interstitial nephritis upon which a marked acute process is grafted, we *must* do without an opiate.

In more than one instance, I fear, I have hastened death through ignorance in permitting its use. When the kidneys are acting well, with little or no albumin, casts, or blood present, if delirium or insomnia are pronounced and threatening, and if other means have failed to relieve, a small or moderate amount of morphine hypodermically is permissible.

Personally, I have never believed in the cold bath, cold pack, or even cold applications locally in the treatment of pneumonia. Occasionally I might permit cold sponging if the fever were very high, but, as a rule, I much prefer the use of tepid or warm water for bathing purposes, to which a moderate proportion of alcohol is added. It seems to me that efforts to diminish fever *per se* in the treatment of pneumonia are scarcely ever a primary and essential object, because I do not believe, as a rule, that the muscular changes produced by increased temperature in its relatively short duration, although very high at times, can be very pronounced; and I believe the nervous shock caused by the toxin is better allayed with slight or moderate heat than with cold.

For a somewhat analogous reason I am opposed to all large doses of quinine to abate pneumonia or to act as a pronounced antipyretic during the course of pneumonia. On the other hand, I thoroughly believe in moderate doses of quinine when well tolerated by the stomach, as a tonic, as a slight antipyretic, as a blood disinfectant, throughout the course of pneumonia. In large doses, while quinine does diminish temperature, it also decreases heart power and general strength, and, therefore, is prejudicial to the patient's well-being. Be it added, however, that quinine as an antipyretic for those who wish to follow out this indication formally is far less dangerous in use than antifebrin, antipyrin, or even phenacetin.

I am of the opinion that there is weighty evidence to prove that the solution of ammonia is a preparation, used moderately and continuously in pneumonia, of considerable value. Its value is specially shown not as a stimulant—because in that particular I believe alcohol, as whiskey or brandy, to be more desirable—but to keep the blood alkaline and fluid. In this disease, especially in the grave

forms and where there is extensive pulmonary consolidation, it is to my mind a very important matter. I have seen many patients in whom, before death and at the autopsy, I have been convinced that heart clot avoided would possibly or probably have meant a life saved. To no one as much as to Benjamin Ward Richardson is the honor due of great insistence upon this important fact, too much ignored to-day in medical writings and medical practice.

Large doses of digitalis at any period of the disease are, as I believe prejudicial to the patient and can never do good. In the milder forms of the disease they are not even indicated from any point of view; in the graver forms and in middle adult life, particularly of most city men, arterial changes counterindicate its use, not to speak of possibly granular degeneration of cardiac muscular fibre. Frequently I have seen the pulse become rapidly very tense and more or less irregular under its use, and the heart action tumultuous, irregular, and forced, as it were, uselessly and vainly. Minute continuous doses of digitalis, given before there are any symptoms of heart failure may prove useful in warding it off, and, when heart failure shows itself not discontinued but protected as to its action upon peripheral arteries, with a moderate amount of nitroglycerin, $\frac{1}{200}$ or $\frac{1}{100}$ grain given every two or three hours, I have found useful, I am confident.

We must bear in mind always that digitalis is not the drug from which we should expect good effects very rapidly in the treatment of pneumonia. Its action, to be useful, must have time as an element, and if given in small doses its cumulative effects, by reason of slow elimination, do not become prejudicial. Apart from other considerations, digitalis in anything but small doses will often cause stomachal intolerance. So soon as there is evidence of pronounced cardiac weakness, digitalis, or, much better, good digitalin and strychnine, should be given hypodermically, and not by the mouth. Medication by the mouth in grave conditions in pneumonia is uncertain and unreliable, except for alcohol and possibly nitroglycerin, which do not derange the stomach, and hypodermically may cause considerable local irritation.

In regard to strychnine, while I value it highly in the treatment of pneumonia, I am satisfied we have to-day often pushed its use to an extreme degree, and in more than one instance in which a $\frac{1}{30}$ or even $\frac{1}{20}$ grain had been used hypodermically every two or three hours, I have cried a halt, because I was satisfied insomnia and delirium were being aggravated and the heart action not in reality stimulated by this overdose. I am inclined to believe that my friend Dr. R. G. Curtin has struck a warning note in this connection which the profession will do well to consider and be guided by. In more than one instance in the treatment of pneumonia, and where other heart stimulants had been of little or no avail, I am sure I have been of use and helped save life with the use of the best available prepa-

ration of coca. Given by the mouth or hypodermically, it has often been of service when I had almost given up hope. The reason, I believe, that this agent does not more frequently respond to our wishes is because the preparation employed is relatively inert. Many coca leaves, not to say the far greater majority, are dry and of poor quality when first gathered. Further, the wrong variety of leaf from which to obtain the tonic alkaloid of the plant is usually employed. Hence, much of the coca used, as wine or extract, contains a large percentage of cocaine, which I believe has little or no tonic properties, and does not contain the other derivatives most valuable in cardiac exhaustion of pneumonia. Here is not the time or place to speak further on this topic. It is wisdom to give black coffee frequently in advanced cases of pneumonia with evidence of heart weakness or cardiac degeneration, whenever our coca is unreliable, either by mouth or rectum.

There can be little doubt that saline solution infused by the veins or by hypodermoclysis or by the rectum, after a moderate bleeding, has been useful in some instances. I must give a warning note as to using too much saline solution by the veins or too rapidly. I have seen death thus occasioned, as Tyson has also, presumably by dilatation of the right heart.

There is no doubt in my mind that oxygen given frequently from the time pneumonia shows marked gravity is extremely beneficial in many instances; but to be of real value it must be given freely and with unstinted hand, and not begun when death is near and already the patient almost moribund. As to a good preparation of oxygen causing notable bronchial irritation, as is sometimes stated, this I have rarely seen, if at all.

There is a point to which I would refer in connection with treatment, because from its appreciation may proceed, I trust, something of real value in prevention of imminent danger. Absence of leukocytosis in acute lobar pneumonia presages death, as hitherto observed. It behooves us, therefore, to have a careful, differential blood count made as soon as the disease is at all clearly defined; and no matter how limited locally the disease may be for a while, or how little threatening at first the symptoms, we cannot be too solicitous or too careful in such cases in our care and treatment. Several times death has followed rapidly, in my experience, and except for the known result of the blood count I should have been lulled into a false security. Later, also, we may obtain facts of great value from the differential count of the leukocytes, as we now do in appendicitis. If in the beginning, for example, we discover the polynuclear neutrophiles in relative excess and the eosinophiles notably decreased or absent, may we conclude that these are, in reality, the very serious cases, "whether associated with an increase of the total number of the leukocytes beyond the normal or not?" I must leave a positive answer for the while with my laboratory friends.

I am of the opinion that except in the beginning of a pneumonia, and in specially rugged or full-blooded patients, venesection is not desirable, as a rule. To this there is one exception. In the first two or three days of the attack of acute lobar pneumonia where general œdema of the relatively healthy lung occurs, I have known life to be saved more than once by a prompt and sufficient venesection (eight to twelve ounces as a mean). Later in the disease, while at times it might be indicated and performed, the result would rarely prove beneficial for more than a very brief period. I grant only two exceptions at an advanced stage. One is, where the right heart is distended and unable to cope with its fluid contents, and despite all judicious cardiac stimulation, the use of nitroglycerin, oxygen, etc.

In these instances I have seen temporary good effects produced by a venesection, and occasionally, perhaps, a life saved. The distention of right heart and jugulars, with great breathlessness, pallor, or almost lividity of lips, face, extremities, and even portions of the trunk, means beginning thrombosis, and reducing the bulk of blood will not save life unless we dilute it, and incidentally, perhaps, partially neutralize its contained toxins. Give, therefore, a moderate saline infusion after the venesection, with this hope, and also insist upon beginning immediately or continuing frequently the use of ammonia under form of the strong solution or the aromatic spirits.

The other condition in which venesection may be and is occasionally useful is where the patient is suffering unquestionably and mainly from profound general toxæmia. It is then an indifferent matter, relatively, whether the pneumonia be in its initial stage or fully developed. In the latter stage of the disease, as in the former, I should usually consider it indicated to make a moderate infusion of saline solution by the veins, or give the solution by hypodermoclysis, or by repeated enemas or irrigations, to dilute the poisons remaining in the blood. I insist, however, that the quantity of the venous infusion in these and all instances should be moderate and the infusion slowly made; otherwise the benefit derived from the venesection will be rapidly neutralized and the patient's immediate condition rendered even worse than prior to the active interference. In one case that comes vividly to mind I felt satisfied that the excessive and too rapid infusion certainly hastened the fatal termination of the case. After the venesection the patient showed signs of returning consciousness, although just before in active delirium, and the pulse was decidedly stronger. A little later, after the venous saline infusion, unconsciousness returned, and the pulse lost strength perceptibly and rapidly until death supervened.

There are good reasons at present to support my contention, particularly in pneumonia. In this disease there is a notable retention of chlorides; hence we should not add much to these, especially where there is doubt as to the condition of the kidneys. If there be

marked epithelial changes in these organs, which as we know not infrequently exist in severe cases of lobar pneumonia, rapid œdema of the lungs may be effected, which shall prove to be the immediate cause of death, or of an œdema of the meninges or other serous membrane, which may cause a rapidly fatal termination of the case.

The quantity of water may do harm. Whenever saline infusion is followed by marked diuresis we are apt to obtain good effects; but in other instances we find the contrary prevails and certain accidents occur. Some of these, due to a further retention of chlorides, I have already referred to. But we may have others, occasioned especially by the amount of the fluid itself, which are dilatation of the right heart, followed by cardiac failure; vascular distention in the lungs and, as a result, great dyspnœa, accompanied or not by pulmonary œdema, and uræmic symptoms of imminently grave import, the explanation of which is probably multiple. Suffice it to add that saline infusions, moderate in quantity and slowly made, are cardinal indications in my judgment, at present, whenever this treatment is seemingly called for in the treatment of lobar pneumonia.

It may be that in certain instances it would be well even to substitute the sulphate infusion for the chloride, in view of the injurious known results of the latter at times, and although the quantity infused is moderate. This problem is still *sub judice.*

No doubt in the beginning of the attack of acute lobar pneumonia it is useful to prescribe a few grains of calomel to free the intestinal tract, thus lessening local congestion of the lungs and eliminating a certain amount of toxins. Aside from this it is claimed that a dose of calomel, if sufficiently large and employed properly, may act as a local disinfectant of mouth and throat (Musser), and later, in like manner, in stomach and bowels. At an advanced stage of the disease we all know what extreme gravity is connected with great distention of the bowels, whether it acts mechanically by pressure upon heart and lungs, and thus prevents their functions being exercised, or by reason of great absorption of toxins from the bowels, increasing notably this source of peril to the patient. In either event we have often a paralytic condition which aids further distention and is only too evident and threatening. When this condition occurs we should first of all empty the bowels by a proper dose of some mercurial, preferably calomel or a gray powder or a saline aperient, and afterward give a pint or two of normal hot saline solution as an injection, which may be repeated twice or more times in twenty-four hours. Not only is much decomposing and poisonous excreta thus carried off, but, in addition, through absorption, the toxins in the blood are diluted and rendered more bearable by the patient, and at the same time the heart action is strengthened and the renal secretion rendered more active.

By some we know the kidneys are considered the most powerful emunctory of the economy in acute lobar pneumonia, and whenever

the urine diminishes notably in amount and there is great decrease in contained chlorides, the indication is to awaken their action and proper secretion as rapidly as possible. Saline irrigations or injections, administration of salt in the food, supplies as far as may be at times two formal objects of treatment. When these fail we may give, by the mouth in proper form and dose, some intestinal antiseptic drug like betanaphthol, the salts of bismuth, creosote, charcoal, or a mineral acid, and obtain a good result.

Upon such medication in like case, I confess, I place but small reliance, in view of the evidences in all organs and functions of the intense and very grave toxæmia of the pneumonic infection.

A final word in regard to the use of alcohol in pneumonia. To my mind there can be little doubt that acute lobar pneumonia is one disease at least in which the use of alcohol is almost imperative at times if we wish to tide the patient over an imminent crisis. The frequency and amounts given at such times are governed almost solely by the urgency of the case and the apparent benefit derived. Under other conditions, especially with those unaccustomed to the use of alcohol when well, the amount given may be small or *nil*. With alcoholic subjects, of course, alcohol must be allowed freely, even though the disease may not be far advanced nor very threatening, except from our previous knowledge of how much such cases are always grave. As a matter of great practical importance, I would insist that the whiskey, brandy, or champagne which is taken by the patient should be the best or purest procurable. I am sure many cases of nausea or more pronounced stomachal intolerance, particularly in hospital treatment, are caused by cheap and bad spirits given to the patients. Can anything be worse than such symptoms at a time when the circulation needs all available extra stimulation? And is it not deplorable to think that these are caused or aggravated frequently by meanness or ignorance which permits or upholds the purchase of liquors for the treatment of the ill, of a very inferior grade, and which, in my judgment, are often injurious rather than beneficial.

In the treatment of no disease are frequently repeated visits from the physician, supported from the beginning with good nursing, more important than in that of pneumonia. In no disease, therefore, is free and unstinted expenditure of money more serviceable. Attention to these requirements will be the means of saving many lives which otherwise would be surely lost.

In conclusion, I wish again to emphasize what I regard as essential propositions. These are:

1. To begin judicious, rational treatment immediately and to continue it during the attack.

2. The most useful *single agent* in treatment, as preventive and curative, is creosote, used preferably as inhalations, properly given and continued for a sufficient length of time.

3. Strict avoidance of extremes of treatment in any direction, whether it be toward the use of so-called specifics or the employment of certain drugs, notably digitalis and strychnine.

4. It should be graven on our minds that pneumonia may be throttled or minimized most surely in the beginning. Later, when the disease is fully developed, our role is inferior, but should consist mainly in doing least harm.

5. Harm proceeds almost invariably from ignorance or undue enthusiasm.

CEREBRAL SKIAGRAPHY.[1]

By G. E. Pfahler, M.D.,
of Philadelphia,
Formerly Assistant Chief Resident Physician in the Philadelphia Hospital; Assistant Physician and Skiagrapher to the Medico-Chirurgical Hospital; Lecturer upon Medical Terminology and Symptomatology and Demonstrator of Physical Diagnosis in the Medico-Chirurgical Hospital.

The Secretary has invited me to read a paper upon the above subject, and for this purpose I have selected 30 skiagraphs from a series of about 100 brain examinations, and have had lantern slides made for demonstration. The lantern slides, like the prints, do not show the detail that is found in the negative.

Some of the examinations have been made upon the cadaver and some upon the living subject.

I have omitted the clinical symptoms and observations. I have done this partly for the sake of brevity and partly because the histories have been or will be published elsewhere by the physicians in attendance.

My first case was a woman, aged thirty-two years, in the Philadelphia Hospital, in which Dr. Charles K. Mills had located a brain tumor by clinical symptoms and observations.[2] Through the kindness of Dr. Mills I was permitted to make an *x*-ray examination, with the idea of testing its value as a means of diagnosis.

The site of the tumor was located clinically in the left parietal region, possibly invading the motor region, and extending to or compressing the posterior limb of the internal capsule and the optic radiations where they approach one another in the region of the basal ganglia.

The left side of the head was therefore placed upon the plate, and the anode of the tube was placed directly opposite to the point

[1] Read before the annual meeting of the American Roentgen Ray Society, at St. Louis, September 8–13, 1904.

[2] Philadelphia Medical Journal, February 8, 1902.

at which Dr. Mills had located the tumor. An exposure of four minutes was made with a current of about six ampères and a tube, the vacuum of which corresponded to about two and one-half inches of air gap.

A negative was obtained which showed good detail of all the structures, namely, the scalp, the outer table of the skull, the diploë, and the inner table, the frontal, ethmoidal, sphenoidal, and mastoidal cells, the coronal suture, the groove of the posterior meningeal artery, the outline of the base of the skull, and shadows corresponding to the depressions for the frontal convolutions, and a large shadow, lying between the coronal suture and the posterior branch of the middle meningeal artery, corresponding to the area in which Dr. Mills had located the tumor.

For comparison, a colored woman of the same age was then selected, and a similar examination of the brain and skull made. This negative showed the normal structures, but did not show the shadow of the tumor seen in the negative of the first case, but did show diffuse shadows throughout the cerebral portion. These can probably be accounted for by the thickness and density of the skull, which is indicated by the thickness of the outer table, which is shown, and by the absence of all of the sutures and meningeal grooves. The absence of these lines is not due to a poor negative, as is shown by the fact that good definition is obtained of the structures at the base of the skull.

I then confirmed these observations by repeating the examination in each patient.

An operation was decided upon and performed by Dr. Hearn and Dr. Da Costa. They removed the part of the tumor corresponding to the upper portion of the shadow. The remainder was removed at autopsy, and was found to be subcortical and corresponded to the remainder and less dense part of the shadow.

At the suggestion of Dr. Mills, I then made some experiments upon the cadaver. The first subject was a man, aged sixty-three years. I hoped to show that a tumor could be shown in any of the usual locations. The usual incision for the removal of the scalp was made, and the left half of the cranial vault removed, leaving the right intact. Without disturbing the brain, and carefully replacing the section of bone and suturing the scalp, I made a negative, to show the normal shadows of this particular skull and brain (Fig. 1). I then removed a section of brain corresponding to a hardened cerebellar tumor, the specimen being from a case reported by Dr. J. Hendrie Lloyd. I placed the tumor in the cavity made for it and replaced the section of bone and sutured the scalp, so as to preserve as nearly as possible the conditions that would be found in the living subject. The negative made showed a very distinct shadow of the tumor.

The tumor was removed from this site and placed in the frontal

region, having for its boundary the first left frontal convolution, and for its posterior boundary the central fissure. The brain tissue was replaced in the first site and a negative made which showed the tumor, but with less dense shadow than in the first position. This was probably due to a more penetrating light. This negative showed the absence of brain tissue where it had not been cut to fit the tumor exactly.

Fig. 1.

Normal skull and brain.

The tumor was now placed in the posterior portion of the left hemisphere, the frontal section replaced, a negative made, and the skull and scalp closed as before. This negative not only showed the tumor, but also the outline of the section of brain in the frontal region which had been replaced.

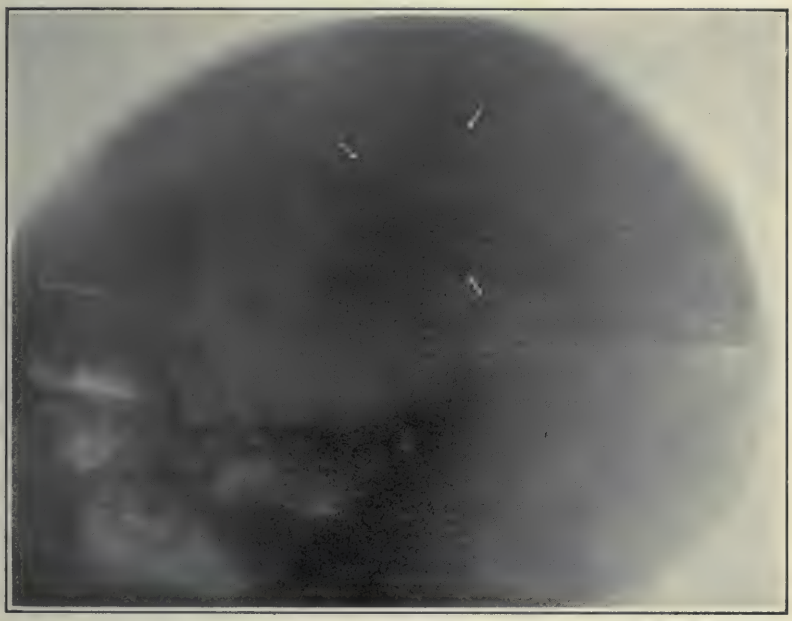
Dr. Mills and Dr. Spiller reminded me that a hardened tumor in a fresh brain might not be a fair test. To harden it the brain was placed in a 10 per cent. formalin solution for fifteen hours. It was then returned to the skull and the tumor replaced in the motor region. A good shadow of the tumor was obtained, and the markings of each section of the brain tissue previously made were shown (Fig. 2).

My second subject was a white woman, aged twenty-nine years. In this series I hoped to show that a cerebellar tumor could be

shown, and also that the different varieties of tumors could be photographed. I used all the free tumors obtainable. The first was a cerebellar sarcoma from a case studied by Dr. James Hendrie Lloyd, the specimen being preserved in the Pathological Museum of the Philadelphia Hospital.

The tumor was placed as nearly as possible in the same position as it had been found in Dr. Lloyd's case. A definite shadow of the tumor was obtained. I then used a perithelioma which had been removed from a case of Dr. Mills. The tumor was skiagraphed in the central part of the motor area. The next was an endothelioma

FIG. 2.



Location of tumor is indicated by the arrows. See location of the cuts into the brain tissue, in the posterior frontal region, there being no actual loss of tissue.

loaned by Dr. Spiller. This was also placed in the motor area and a shadow obtained of only slightly greater density than that of the surrounding brain tissue, but the sections of the tumor itself were shown. In another experiment a large spindle-celled sarcoma of the pineal gland was placed in the motor region and a shadow obtained.

In all of these series the plates were overexposed, though the time had only been four minutes in each case. I then repeated the series upon the body of a man, aged fifty-four years, timing the plates three minutes, with the result that all were underexposed. Still feeling that my results might be questioned, because I had used

a hardened tumor in a fresh brain, I used the following test and repeated it: Half of a fresh brain was taken and placed beside the half of a hardened brain and the two photographed with the hardened tumor on the same plate and under the same light. The hardened brain was a little larger than the fresh one. The negative showed more detail in the hardened brain, but the density of the shadow was little if any greater than that of the fresh one. The shadow of the tumor was more dense than either one.

Realizing that much of the success in skiagraphy of the brain must of necessity depend upon accurate technique, I therefore conducted a series of experiments to find the best possible technique. In skiagraphy we have five principal varying factors. These are the distance of the anode from the plate, the time of exposure, the vacuum of the tube, the amount of current, and the thickness and density of the part examined. The first four are more or less under our control. The fifth is always variable, and, therefore, the other four must be judged and regulated in proportion to the fifth. Fortunately, the variability in the thickness of the adult skull is not very variable, but must not be entirely ignored.

In this series of experiments I used at one and the same time three different tumors, one a spindle-celled sarcoma, one an epithelioma, and one a perithelioma. One was placed in the prefrontal region, one in the motor region, and one between the two halves of the cerebellum. My first series of plates was made to determine the best time of exposure. In this test I used a tube the vacuum of which was equal to two and one-half inches of parallel air-spark at a distance of eighteen inches, and as the subject I had the body of a woman, aged forty-two years. The time of my exposures were two, two and one-half, three, three and one-half, and four inches, respectively.

My best results were obtained with an exposure of three and one-half minutes.

I then made a series of negatives in which the distances of the anode from the plate were twelve, fifteen, eighteen, and twenty-one inches, respectively. My best results were obtained at a distance of eighteen inches. At this distance the shadows of the proximal side of the skull will be more or less diffused, and yet sufficient detail of the opposite half of the brain be obtained.

The degree of vacuum is our most variable factor and the one that is least under our control, and, therefore, experience and judgment in varying the other factors accordingly will have an important bearing upon the results in each case. I used a self-regulating tube and used as nearly as I could vacuums corresponding to two, two-and-one-half, three, and three-and-one-half inches of parellel air-spark.

My best results were obtained with a vacuum of two-and-one-half inches.

The developer that I used was the following:

A.—Metol	4 drachms.
Hydrochinone	4 "
Sodii sulphite	5 ounces.
Water	5 pints.
B.—Sodii carbonate	4 ounces.
Water	30 "

Use two parts of A. and one of B.

These experiments were made about three years ago, while I was at the Philadelphia Hospital. At that time I was using a fifteen-inch coil with a mechanical interrupter, and used a current of 8 to 10 ampères. With our modern technique and modern coils the time must be reduced. At the present time I make my exposure one and one-half minutes, with 8 to 10 ampères and the mechanical interrupter, or in forty-five seconds with the electrolytic interrupter and 25 ampères.

Since the above experiments I have had the opportunity of making a fairly large number of brain examinations. Most of them were obscure cases. Several of these are worthy of mention.

One, a case of Dr. Charles K. Mills,[1] in which the *x*-ray examination showed the normal details of the skull, and, in addition, showed an abnormal shadow about three inches in diameter and irregular in outline lying directly in the motor region. This was interpreted as the shadow of the tumor, and corresponded to the clinical diagnosis. The shadow of the inner table of the skull was seen to be interrupted in the region of the tumor and seemed to be disorganized. At the time of the operation, by Dr. John B. Deaver, the inner table was found to be diseased and gave rise to considerable hemorrhage. The tumor was removed and found to correspond in size and position to the shadow in the skiagraph.

In another case of Dr. Mills,[2] which was of unusual interest, the skiagraphic examination showed the shadow of a gumma in the motor region of the left side of the brain. The shadow was two and one-half inches in length, one and one-half inches in width at its widest portion, irregular in outline, and, from its density, I estimated it to be about one-half inch in thickness. The gumma when removed by Dr. Hearn and Dr. Da Costa corresponded exactly to the location and dimensions given in the skiagraphic examination (Fig. 3).

There are several other cases of brain tumor in which the diagnosis has not been decided by either operation or autopsy, and, therefore, of little value scientifically. One of these is a case referred by Dr. C. A. Veasey for *x*-ray examination.[3] He had suspected a tumor of the pituitary body, because of bitemporal hemianopsia.

[1] Philadelphia Medical Journal, September 27, 1902.
[2] Ibid., November 29, 1902.
[3] Transactions of the American Ophthalmological Association, 1904.

The skiagraph showed a slight shadow, about one-half inch in diameter, and located in the region of the pituitary body. This shadow must, of course, only be accepted as confirmatory, and not in itself diagnostic. In fact, if it did not agree with the clinical symptoms, I should ignore it, for such a small tumor located in the central portion of the brain could not be expected to cast a definite shadow.

We sometimes learn more from our failures than from our successes, and, therefore, I desire to mention an instance in which I was mistaken recently. The case will be reported in detail later, and, therefore, I shall only note it in so far as it has a bearing upon

Fig. 3.

Case of Dr. Mills. Gumma indicated by the arrows.

the subject under consideration. The case was referred by Dr. B. F. Hawley and Dr. Judson Daland. A brain tumor was suspected, but the symptoms were obscure, and no definite diagnosis could be made. The skiagraph showed a large shadow occupying in part the region of the cerebellum and in part the posterior portion of the cerebrum. An operation was performed by Dr. W. W. Keen, and no tumor was found. Autopsy showed no tumor in this region, but showed a tumor, about one and one-quarter inches in diameter, lying farther anteriorly. The autopsy was performed by Dr. W. G. Spiller, at which I was priviledged to be present. There were several other very small tumors found, but nothing was found

either in the skull nor in the brain to account for the shadow that I had obtained. I was very much disappointed and puzzled. I believe, however, that this shadow was produced by the greater diameter of the head at this point and by the contact of the head at this point which I find interferes with the developing. Allowance must always be made for these shadows. This was only half of an explanation, since it did not account for the fact that I did not find the tumor where it was located. Through the kindness of Dr. Spiller, I was permitted to examine the brain skiagraphically. I made several lateral and vertical views. Beautiful details of the lobes and convolutions and of the ventricles of the brain were

FIG. 4.

Case of Drs. Hawley and Daland. Skiagraph of the brain, post-mortem. Tumor indicated by the arrows.

obtained. The shadow of the tumor could be recognized, but the density of this shadow was so little greater than the surrounding brain tissue that I feel sure it would have been impossible to locate it skiagraphically while in the skull. The skiagraphic examination may still be of value in distinguishing this variety of tumor from others (Fig. 4).

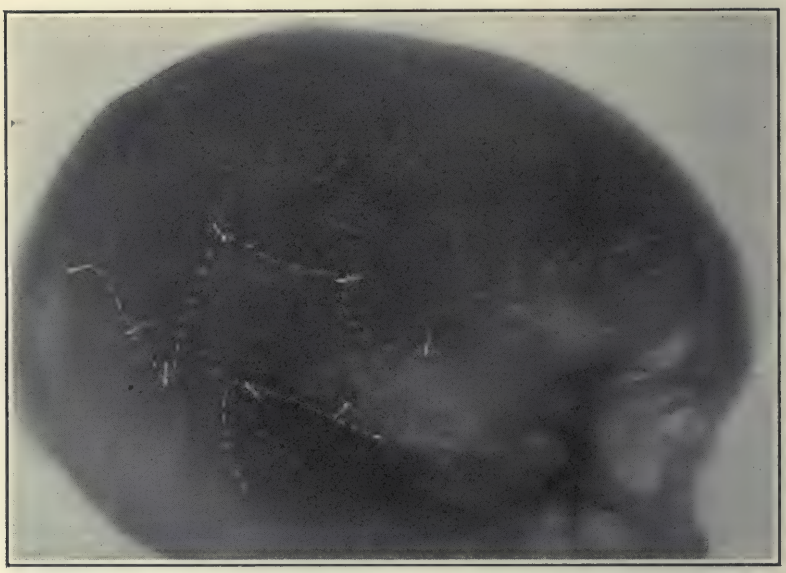
In addition to the brain tumors studied, I have had the opportunity to examine three cases of softening of the brain. Two of these were examined post-mortem, and one was examined during life and the diagnosis confirmed by autopsy.

The first was Dr. Charles W. Burr's case.[1] The case was one of

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, February, 1904.

thrombosis of the midcerebral artery, with cystic degeneration, and causing aphasia and hemiplegia. The examination was made post-mortem. The brain was replaced and the skull and scalp closed. I then made a negative of the affected side and also of the opposite side, because I believed that possibly the normal side could be compared with the affected sides. This case, however, demonstrated that this cannot be relied upon, for the lesion was shown upon both negatives, but with much more definite outline on the affected side. The skiagraph showed above the cerebellum and petrous portion of the temporal bone a light area which corresponded exactly with

FIG. 5.



Dr. Burr's case. Area of softening is indicated by the arrows.

the outline of the area of degeneration. This skiagraph showed, also remakably well the convolutions of the cerebellum (Fig. 5).

The second case was also one of Dr. Burr's, in which an irregular area of degeneration was found in the distribution of the mid-cerebral artery and which had caused hemiplegia. The skiagraph showed transparent areas which corresponded exactly with the area of degeneration (Fig. 5).

The third case was a very interesting case of aphasia, in the Insane Department of the Philadelphia Hospital, which was studied very carefully by Dr. Charles K. Mills.[1] Two skiagraphs made at intervals of several months showed a light area about one inch in diam-

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, September, 1904.

eter (Fig. 6), located in the region of the speech centre. The autopsy showed a corresponding area of softening involving the posterior portion of the third left frontal convolution and the island of Reil.

Some of the results obtained in skiagraphy of the brain have been most surprising and gratifying both to myself and others. Other results have been most disappointing.

Dr. Church, of Chicago, records a case of cerebellar tumor in which the x-rays were used by Mr. W. H. Fuchs. Skiagraphs of the tumor were obtained. At autopsy a highly vascular gliomatous

FIG. 6.

Dr. Mills' case. Area of softening is indicated by the arrows.

tumor was found, the tumor being the seat of several old and recent hemorrhages, and also of a recent clot of considerable size.[1]

Obici and Ballici[2] demonstrated, by means of the x-ray the presence of tumor in a case of a boy who died of brain tumor, the experiment being performed post-mortem. They also experimented with tumors of different kinds placed in the brain of cadavers, and were, in some instances, able to obtain localizing shadows.

Oppenheim,[3] in reviewing the subject of brain tumors in his text-book, says that his attempts to use the x-ray for diagnostic purposes

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, February, 1899.
[2] Rivista di Patholog, October, 1897. Cited by Church.
[3] Diseases of the Nervous System. Translation by Edw. Mayer, M.D., Philadelphia and London, 1900.

failed, although he was able to determine that a tumor placed within the cranium upon the brain was very distinctly noticed.

Pancoast and McCarthy conclude that the value of the Roentgen rays in brain lesions is at present dubious.[1]

In addition to the tumors and cases of softening, I have had a case in which the skiagraph seemed to show thickening of the membranes to a considerable extent. This corresponded to the clinical symptoms. No autopsy has been obtained, and, therefore, I can draw no definite conclusion.

In conclusion, I believe that we should be able to show in the skiagraph most large lesions, such as new-growths, softening, hemorrhage, and abscess; but I want to repeat what I said at our meeting a year ago, when discussing this subject, "I would never take the responsibility of an operation upon the brain purely upon skiagraphic evidence.

"On the other hand, all of the above cases should be examined by the *x*-ray, with the idea of confirming or adding to the clinical evidence."

ON THE PRESENCE OF ORGANIC ACID IN THE URINE IN CASES OF RHEUMATOID ARTHRITIS.

By Helen Baldwin, M.D.,
of New York.

(From the Laboratory of Dr. C. A. Herter, New York.)

While rheumatoid arthritis presents such marked and distinctive pathological features, its etiology and the primary seat of the affection are still unknown. Because of this the study of the metabolic changes taking place in the course of the disease becomes of especial interest, and any observation seemingly of small moment may prove of real value in helping to determine the cause of the morbid condition.

It is with this in view that the following observations are recorded, relating to the presence of an organic acid in the urine of patients suffering from this disease.

From the time of the first examinations of urinary sediment with the microscope, the presence of certain organic acids in the urine has been recognized. Uric acid, oxalic acid, and hippuric acid, by their precipitation under morbid conditions, have been forced upon the attention of pathologists, and in the study of methods for their

[1] University of Pennsylvania Medical Bulletin, March, 1903.

estimation it was early found that they were present in the urine in solution even when not found in the sediment. It was not, however, until the study of acid intoxications by Gaethgens,[1] Walter,[2] Salkowski,[3] and later others, as Stadelmann[4] and Magnus-Levy,[5] that methods were discovered for detecting organic acid in the urine and approximately estimating the amount present even when the nature of the acid was not known.

The method employed by Magnus-Levy[6] in determining the amount of β-oxybutyric acid excreted in diabetes is the one which has been used in making the following observations. This method is based upon the fact which has become well established that acids are excreted from the kidneys, not as free acids, but only in combination with bases to form salts. This being the case, if all the acids and bases present in the urine are estimated and represented in terms of their chemical equivalents, with reference to the same substance as sodium, the total acid present will be found to exactly balance the sum of the bases. Gaethgens, Hagentorn, and Magnus-Levy found that when the known acid and basic constituents present in appreciable quantities in normal urine were thus estimated, the acids and bases did almost exactly balance each other. There was, however, uniformly present a slight excess of acids over the bases determined, and this was considered to be balanced by organic bases such as the purin bodies, which had not been estimated. Estimations were made of potassium oxide, sodium oxide, calcium oxide, magnesium oxide, and ammonia, and of hydrochloric acid, uric acid, preformed sulphuric acid, combined sulphuric acid, monobasic phosphoric acid, and dibasic phosphoric acid.[7]

[1] Zur Frage der Ausscheidung freier Säuren durch den Harn. Med. Centralbl., 1872, S. 833. Ueber Ammoniakausscheidung, Zeitschr. f. physiolog. Chemie, Bd. iv. S. 35.

[2] Untersuchungen über die Wirkung der Säuren auf den thierischen Organismus, Archiv f. experiment. Pathol. u. Pharmakol., 1877, Bd. vii. S. 148.

[3] Ueber die Möglichkeit der Alkalienziehung am lebenden Thiere, Virchow's Archiv, 58, S. 1.

[4] Ueber den Einfluss der Alkalien, u. s. w., Stuttgart, 1890, S. 122 ff. bei Hagentorn.

[5] Die Oxybuttersäure und ihre Beziehungen zum Coma diabeticum, Archiv f. experiment. Pathol. u. Pharmakol., 1899, Bd. xlii. S. 149. Untersuchungen über die Acidosis im Diabetes mellitus und die Saureintoxication im Coma diabeticum, Archiv f. experiment. Pathol. u Pharmakol., 1900–1901, Bk. xlv. S. 388.

[6] For a detailed discussion of this method reference is made to Magnus-Levy's article, loc. cit.

[7] The following methods were employed in estimating the acids and bases. (See Neubauer und Vogel's Harnanalyse.)

Potassium and sodium by Lehmann's method. Separation by indirect volumetric method.

Calcium oxide, by precipitating as CaC_2O_4 and weighing as CaO.

MgO, by precipitating as NH_4MgPO_4 and weighing as $Mg_2P_2O_7$.

NH_3, by Schlösing's method.

SO_3 preformed and SO_3 combined, by Salkowski's gravimetric method.

P_2O_5 total, by Neubauer's volumetric method.

P_2O_5 dibasic and monobasic, by Freund's method.

Cl, by Mohr's method.

Uric acid, volumetrically by Folin's method. Zeitschr. f. physiolog. Chemie., Bd. xxxii. S. 514.

The following cases from our records illustrate the balancing of acids and bases in twenty-four-hour specimens of normal urine.[1] The weights are given in the sodium equivalent of each acid or base (Table I.):

TABLE I.

Case	I.	II.	III.	IV.	V.	VI.	VII.	VIII.	IX.	X.
K_2O	2.525	1.547	2.5720	1.0470	0.7286	1.2840	0.9232	1.6360	2.3740	0.9757
Na_2O	2.001	4.249	5.2250	2.4040	1.3300	2.1090	3.881	3.7040	4.0930	1.2970
CaO	0.2165	0.476	0.2289	0.0126	0.0768	0.0722	0.2154	0.2319	0.0952	0.0307
MgO	0.1439	0.268	0.1302	0.1298	0.0664	0.1757	0.0806	0.1733	0.2237	0.1098
$N(H_3)$	0.6127	1.398	1.3910	0.3136	0.2859	0.4561	0.4704	1.5430	1.0930	0.5181
Total bases	5.4991	7.938	9.5471	3.9070	2.4877	4.0970	5.5706	7.2882	7.8789	2.9313
SO_3 preformed	0.9051	1.420	1.5390	0.5584	0.4709	0.7078	0.9734	1.4500	1.2880	0.6570
SO_3 combined	0.0465	0.073	0.1347	0.0219	0.0150	0.0167	0.0356	0.0564	0.0663	0.0243
P_2O_5 dibasic	1.300	0.782	1.1930	0.5864	0.4808	3.0730	0.7432	0.8680	0.7387	0.4212
P_2O_5 monobasic	0.0849	0.601	0.3023	0.0408	0.0548	0.0364	0.1987	0.3715	0.2916	0.2106
Cl	3.171	5.386	6.9720	2.8280	1.5180	0.5994	4.476	4.5910	5.4130	1.6360
Uric acid	0.0432	0.117	0.0894	0.0221	0.0143	0.0930	0.0584	0.0911	0.0870	0.0431
Total acids	5.5507	8.379	10.2304	4.0576	2.5538	4.5263	6.4853	7.4280	7.8846	2.9922
Apparent excess of acids balanced by organic bases	0.0516	0.441	0.6833	0.1506	0.0661	0.4293	0.9147	0.1398	0.0057	0.0609

If, now, an acid is excreted in the urine other than those ordinarily found its presence can be detected in estimating the acids and bases, for in this case there will be an excess of bases over the acids normally present, the excess being required to neutralize this acid, which is not normally excreted. This may be illustrated by a twenty-four-hour specimen of urine from a case of diabetes mellitus. The patient had 5 per cent. of sugar in the urine.

The analysis is as follows, the weights as before being in equivalent weights of sodium:

K_2O	5.0070 grms.	SO_3 preformed	1.5950 grms.
Na_2O	6.5030	SO_3 combined	0.0666
CaO	0.2051	P_2O_5 dibasic	2.0160
MgO	0.3910	P_2O_5 monobasic	0.5054
$N(H_3)$	1.7120	Uric acid	0.1719
		Cl	6.5030
Total bases	13.8181	Total acids	10.8579

The excess of bases over the acids estimated in this case is 2.9602 grams, or 21 per cent. of the total bases; that is, the amount of organic acid present (in this case known to be chiefly β-oxybutyric acid) is that which will combine with 2.96 grams of sodium.

[1] It is, of course, necessary to use the greatest care in preventing any decomposition of the specimens, since the conversion of urea into ammonium carbonate will invalidate the result. The separate portions of urine should be thoroughly shaken with carbolic acid, chloroform, or thymol before any bacterial action can begin.

It is also evident that if any organic acid, as salicylic acid or the salicylates, were administered at the time of the observations, it would be estimated with the other organic acid excreted.

Magnus-Levy used this method chiefly in estimating the amount of organic acid present in diabetic urine. He mentions, however, that organic acid is in this way found to be present in lesser amounts in other conditions, such as starvation, intestinal disturbance, phosphorus poisoning, acute yellow atrophy, and fever. Herter and Wakeman,[1] using Magnus-Levy's method of analysis, reported the finding of organic acid in the urine in cases of dilatation of the stomach, with atony, rheumatoid arthritis, and cirrhosis of the liver.

Since in the cases of rheumatoid arthritis reported by Dr. Herter there was found organic acid in the urine other than that normally present, it has seemed well to continue this investigation. I have, therefore, estimated the acids and bases in the urine in all cases of this kind as patients happened to come under observation.

The following records include reports of forty specimens of urine from twenty-one different patients. In all cases in which the disease was progressing—that is, in thirty-three of the specimens—there was found to be an excess of the bases over the acids normally present, thus indicating the presence of organic acid. The remaining seven specimens were from patients in whom the symptoms were stationary or improving, and in these the analysis showed a normal condition—that is, with the estimated acids slightly in excess of the bases.

In studying these records it should always be borne in mind that an apparent excess of bases indicates the presence of a corresponding amount of some acid not normally present in the urine, and so not estimated.

Case I.—An illustrative case may be reported in detail.[2] The patient was a young woman who for several years had been suffering from rheumatoid arthritis. Both ankles, both knees, both wrists, and the small joints of the hands were involved, with swelling, tenderness, pain, deformity, and impairment of motion. At the time that the first analyses were made the disease was steadily progressing. The results of the urinary analysis were as follows:

October 26, 1899.	K_2O	1.3370	SO_3 preformed	0.9961
	Na_2O	3.9780	SO_3 combined	0.0388
	CaO	0.1345	P_2O_5 dibasic	0.6725
	MgO	0.1861	P_2O_5 monobasic	0.1400
	$N(H_3)$	0.9663	Uric acid	0.0868
			Cl	3.8830
	Total bases	6.6019	Total acids	5.8172

Excess of bases 0.7847, or 11.9 per cent. of total bases.

[1] Notes on Acid Intoxications. Proceedings of New York Pathological Society, 1900–1901. C. A. Herter. The Pathology of Acid Intoxications. Transactions of the Association of American Physicians, vol. xv.

[2] Only a brief summary of the condition of these cases is given, since the question as to whether the disease is progressive or stationary seems to be the one determining whether or not the abnormal acid is present in the urine.

27th. Total bases, 4.7823; total acids, 4.6475; excess of bases, 0.1348; 2.8 per cent. of total bases.

28th. Total bases, 7.9051; total acids, 7.2755; excess of bases, 0.6296; 7.8 per cent. of total bases.

January 20, 1900. Total bases, 5.7926; total acids, 5.1932; excess of bases, 0.5994; 10.3 per cent. of total bases.

At this time the stomach contents were examined, and there was found to be no hydrochloric acid present after a test meal, although there had been no gastric symptoms. Lavage was used about twice a week for the next ten months. At first the stomach contents were always fermented and contained fatty acids, but after routine washings for several months hydrochloric acid was found in the stomach after a test meal.

Urinary Examination. February 14, 1900. Total bases, 6.7765; total acids, 6.1873; excess of bases, 0.5892; 8.7 per cent. of total bases.

April 4th. Total bases, 6.8089; total acids, 6.3930; excess of bases, 0.4159; 6.1 per cent. of total bases.

May 14th. Total bases, 7.2896; total acids, 6.9305; excess of bases, 0.3591; 4.9 per cent. of total bases.

The patient spent the winter of 1900 and 1901 in California, living in the open air and exercising on horseback, with no other treatment. The next analysis was after a year's interval

May 14, 1901. Total bases, 8.0026; total acids, 8.1500; excess of *acids,* 0.1474. At this time the symptoms were all in abeyance. There remained some deformity of the joints and some weakness in the muscles, but the disease was for the time arrested in its course.

Case II.—Another case in which the amount of the abnormal acid was diminished in the urine, with an improvement in the other symptoms, is the following:

The patient was a working girl who had for several years been suffering from increasingly severe symptoms in the joints of the wrists, fingers, knees, and ankles, with characteristic deformities in the joints. She could no longer work, and she could with difficulty walk about.

The stomach contents were examined after a test meal, and there was absence of hydrochloric acid.

Urinary Analysis, February 19, 1900. Total bases, 5.0916; total acids, 4.4570; excess of bases, 0.6346; 12.4 per cent. of total bases.

The patient spent the eight months following this examination under as favorable hygienic surroundings as were possible for a person of small means.

She took hydrochloric acid after meals throughout this time. She markedly improved in health, and became able to use her hands and feet, with but little discomfort.

Urinalysis, November 8, 1900. Total bases, 4.3337; total acids, 4.1108; excess of bases, 0.2229; 5.1 per cent. of total bases.

CASE III.—Another patient showing an improvement in symptoms which was not as marked as in the case of those cited above was the following: On May 24, 1900, the patient was first seen. She then complained of pain in the shoulders, knees, and soles of the feet, with deformity of the hands. Two years before the patient had begun to have severe pain in the hands, extending to the arms. She was unable to sleep on account of the pain, and often walked the floor at night. Then pain developed in the soles of the feet, in the knees, and in the legs. Not until a year later did the joint swelling in the hands begin. There was steadily increasing disability from this time. On examination the hands were found to be in a position of extension and ulnar deflection. Flexion is much limited, extension nearly complete. The lower ends of the ulnar bones are very conspicuous and bulbous. The carpometacarpal joints of the hands are most involved. The right knee is swollen, and there is apparently extra-articular thickening. Extension of this knee is painful. The left knee is not swollen, but is painful on motion. There is no joint deformity in the foot except hallux valgus.

June 7, 1900. The stomach contents, examined after a test meal, showed absence of hydrochloric acid. Total bases in the urine, 5.5391; total acids, 4.4402; excess of bases, 1.0989; 19.8 per cent. of total bases.

The patient improved slowly throughout the summer, but still had a good deal of tenderness in the affected joints when the next examination was made.

December 14*th*. Total bases, 3.0073; total acids, 2.9989; excess of bases, 0.0084; 0.28 per cent. of total bases.

CASE IV.—The following record is that of a patient who was first seen in an interval when she was having no active symptoms. Three years before this she had had rapidly developing symptoms from the disease, with involvement of the knees, ankles, elbows, wrists, and the metacarpophalangeal joints of both hands. At the time when the first urinary examination was made she had remaining some deformity of the joints in the hands, with limitation of motion in the right wrist and left ankle. The urine was at this time normal as regards the balancing of acids and bases. Total bases, 5.0979; total acids, 5.2541; excess of *acid*, 0.1562. Two years after this there was an exacerbation of the symptoms, brought on by exposure to cold. All the joints involved were affected, with very severe pain in the knees on standing and rapid atrophy and loss of power in the muscles. Total bases in twenty-four-hour specimen, 7.9067; total acids, 7.6305; excess of *bases*, 0.2762; 3.5 per cent. of total bases. Five months later, when the acute symptoms were again subsiding, the urine was again normal. Total bases, 4.7278; total acids, 5.1523; excess of *acid*, 0.4245.

The following records are from fifteen cases in which the disease was progressing. It will be noted that in all of these there is an excess of bases over the acids estimated (Table II.):

TABLE II.

	Case V.			Case VI.				Case VII.		Case VIII.	
	Nov. 12, 1900	Dec., 1900	Jan. 31, 1901	Jan. 26, 1900	Jan. 31, 1900	Feb. 21, 1901	4, 1901	Jan. 10, 1900	Apr. 30, 1900	Feb. 11, 1902	Jan. 17, 1903
K_2O	1.1060	0.8600	1.0340	1.027	0.8367	0.9879	0.6258	2.651	2.1200	0.7816	0.5119
Na_2O	2.2730	2.2472	2.4010	1.136	1.2730	0.8217	0.8453	1.013	0.4369	1.992	1.413
CaO	0.1232	0.1290	0.0709	0.1227	0.1039	0.1035	0.1070	0.0605	0.2032	0.0613	0.0821
MgO	0.1915	0.0753	0.0524	0.0350	0.0751	0.0764	0.0903	0.1496	0.1151	0.0814	0.0232
$N(H_3)$	0.4816	0.6272	0.3238	0.6516	0.2541	0.4374	0.2462	0.5401	0.5967	1.298	0.6105
Total bases	4.1753	3.9387	3.8811	2.9723	2.5428	2.4269	1.9146	4.4142	3.4719	4.2143	2.6407
SO_3 preformed	0.4061	0.4949	0.1644	0.4239	0.3238	0.5624	0.3434	0.7177	0.5333	0.6798	0.5501
SO_3 combined	0.0373	0.0335	0.0310	0.0275	0.0305	0.0526	0.0452	0.0600	0.0278	0.0443	0.0455
P_2O_5 dibasic	0.4652	0.4017	0.3889	0.5459	0.1936	0.3286	0.2333	0.6385	0.1313	0.6125	0.9298
P_2O_5 monobasic	0.0259	0.1653	0.0583	0.0428	0.1571	0.2456	0.1846	0.0339	0.1804	0.1531	0.0211
Uric acid	0.0630	0.0420	0.0389	0.0472	0.0302	0.0372	0.0281	0.0433	0.0389	0.0257	0.0821
Cl	2.6180	2.123	2.5540	1.581	1.4870	0.9817	0.8962	2.8000	3.4620	1.954	0.8847
Total acids	3.6155	3.2604	3.2355	2.6683	2.2223	2.2081	1.7308	4.2934	3.3737	3.4694	2.5133
Excess of bases	0.5598	0.6783	0.6456	0.304	0.3205	0.2188	0.1838	0.1208	0.0982	0.7449	0.1274
Per cent. of excess	13.4	17.2	16.6	10.2	12.6	9.02	9.6	2.7	2.8	17.6	4.8

	Case IX.	Case X.	Case XI.	Case XII.	Case XIII.	Case XIV.	Case XV.	Case XVI.	Case XVII.	Case XVIII.	Case XIX.
K_2O	1.3550	1.3385	0.6175	0.7256	1.485	1.558	0.6947	0.9694	0.5495	1.2690	0.8768
Na_2O	3.4010	2.3930	0.9828	3.043	1.088	2.862	4.116	0.8768	3.299	2.1780	1.8980
CaO	0.1184	0.2412	0.2241	0.0634	0.0354	0.2558	0.0952	0.0768	0.1429	0.0965	0.0843
MgO	0.0885	0.1430	0 0746	0.1306	0.1144	0.2125	0.1312	0.0343	0.1432	0.1199	0.1044
$N(H_3)$	1.0440	1.0875	0.5753	0.9131	1.121	1.016	0.2669	0.3861	1.154	0.2226	0.4651
Total bases	6.0069	5.2032	2.4743	4.8757	3.8438	5.9043	5.3040	2.3434	5.2886	3.8860	3.4286
SO_3 preformed	0.6033	0.4935	0.5315	0.6656	0.7519	0.7794	0.2662	0.2433	0.7039	0.4888	0.3082
SO_3 combined	0.0757	0.0463	0.0390	0.0495	0.0372	0.0460	0.0380	0.0409	0.0563	0.0344	0.0321
P_2O_5 dibasic	0.6545	0.6740	0.2522	0.8435	0.6415	1.096	0.5834	0.3796	0.6834	0.6674	0.8035
P_2O_5 monobasic	0.0123	0.0114	0.0074	0.1061	0.1040	0.1801	0.0436	0.0000	0.3095	0.0453	0.0917
Uric acid	0.0586	0.0541	0.0586	0.0456	0.0407	0.0635	0.0891	0.0743	0.2336	0.0090	0.0193
Cl.	3.8780	3.1405	1.0420	3.038	2.129	3.407	3.256	0.7676	3.126	2.1630	1.9110
Total acids	5.2824	4.4198	1.9307	4.7483	3.7043	5.5720	4.2263	1.5057	5.1127	3.4079	3.1658
Excess of bases	0.7245	0.7834	0.5436	0.1274	0.1395	0.3323	1.0777	0.8377	0.1759	0.4781	0.2628
Per cent. of excess	12.1	15	22	2.6	3.6	5.6	20.3	35	3.3	12.3	7.6

Case XVI., which shows the largest amount of organic acid, is that of a very marked case of arthritis deformans in which there was almost complete ankylosis of all the joints. The specimen was examined a few weeks before the patient's death. The urine was alkaline, but showed no evidences of decomposition.

In the two remaining cases, in each of which only a single urinary examination was made, the disease had become stationary. So

while there was much disability and rigidity of the joints, the disease was not progressive. The following records are from these patients (Table III.):

TABLE III.

	Case XX.	Case XXI.
K_2O	0.8461	0.6823
Na_2O	1.489	4.625
CaO	0.1138	0.4042
MgO	0.1695	0.1491
$N(H_3)$	0.6114	1.221
Total bases	3.2298	7 0816
SO_3 preformed	0.5099	1.261
SO_3 combined	0.353	0.0702
P_2O_5 diabasic	0.6234	0 2159
P_2O_5 monobasic	0.1266	0 7511
Cl	1.904	4.865
Uric acid	0.0421	0 0196
Total acids	3.2413	7.1828
Excess of acid	0.0115	0.1012

ON THE OCCURRENCE OF INTESTINAL PUTREFACTION IN RHEUMATOID ARTHRITIS. While the analyses of these specimens of urine were made primarily to determine the relative amount of acids and bases present, there are certain other points of interest with reference to these cases.

Since the work of Baumann it has been recognized that the amount of intestinal putrefaction can be approximately measured by the ratio of the aromatic sulphates to the simple (preformed) sulphates excreted in the urine. Certain aromatic products of intestinal putrefaction, as indol, skatol, and phenol, become linked in the body with sulphuric acid to form the so-called ethereal or aromatic sulphates. Normally these bear a ratio to the simple preformed sulphates of from 1:10 to 1:15, but in cases of intestinal putrefaction the ratio increases to 1:8 or 1:5, or even in exceptional cases, so that the amount of aromatic sulphates is equal to that of the preformed sulphates.

In certain cases of intestinal putrefaction, however, one of these aromatic products may be formed in excess, while the total aromatic sulphates will not be above the normal. Thus the presence of indican in the urine, indicating the formation of indol by a putrefactive process, may be noted in a given case in which the total ethereal sulphates are in normal amount, or the reverse may be true, that indican may be entirely absent from the urine while the formation of other products of putrefaction leads to an excess of aromatic sulphates. In all but two of the cases of rheumatoid arthritis noted above, in which the disease was progressing, there was found either an excess of aromatic sulphates in the urine or else the presence of indican, and these two were mild cases.

In twenty-three specimens there was an increase in the aromatic sulphates excreted, the ratio varying from 1:2.6 to 1:9.8, the average being 1:6.2 (Table IV.):

TABLE IV.

	Case II.		Case III.		Case IV.			Case V.		
	Feb. 19, 1900.	Nov. 8, 1900, improved.	June 7, 1900.	Dec. 14, 1900 improved.	Nov. 15, 1000, no active symptoms.	July 5, 1902, exacerbation.	Nov. 23, 1902, improved.	Nov. 12, 1900,	Dec., 1900.	Jan. 31, 1900.
Volume	1260	740	1400	567	1040	1500	980	1080	900	1120
Specific gravity	1017	1026	1013	1023	1020	1021	1024	1015	1016	1011
Reaction	acid	st'ngly acid	acid	acid	st'ngly acid	acid	st'ngly acid	sl'ghly acid	acid	sl'ghly acid
Albumin	0	0	0	0	0	0	0	0	0	0
Indican	0	...	...	0	0	0	0	...	0	present
Urea	20.03	16.42	22.48	12.17	26.92	33.06	23.4	12.27	14.19	9.85
Uric acid	0.1955	0.4047	0.2072	0.219	0.5618	0.9214	0.5873	0.460	0.3063	0.283
Ratio $\frac{\text{urea}}{\text{uric acid}}$	102	41	108	55	48	36	44	27	46	35
H_2SO_4 preformed	1.7151	1.6063	1.260	1.047	2.068	2.858	1.647	0.865	1.0557	0.350
H_2SO_4 combined	0.1929	0.1307	0.1390	0.083	0.1922	0.2145	0.15	0.158	0.1423	0.132
Ratio $\frac{H_2SO_4\ p}{H_2SO_4\ c}$	8.88	12.28	9.06	12.6	10.8	13.3	10.8	5.5	7.4	2.65
Total N	9.358	7.670	10.51	5.69	12.57	15.42	10.93	5.73	6.627	4.6
N of NH_3 grms.	0.5509	0.4184	0.4387	0.46	0.5025	0.5672	0.3986	0.29	0.3818	0.196
N of NH_3 (per ct. of total N)	5.9	5.5	4.1	8.1	4	3.6	3.6	5	5.8	4.3

	Case VI.				Case VII.		Case VIII.		Case IX.	Case X.
	Jan. 26, 1900.	Jan. 31, 1900.	Feb. 21, 1901,	Mar. 4, 1901.	Jan. 10, 1900.	Apr. 30, 1900.	Feb. 11, 1902.	Jan 17, 1903.		
Volume	600	570	700	530	2095	1815	1120	1250	1335	1033
Specific gravity	1023	1019	1020	1018	1012	1010	.....	1011	1016	1018
Reaction	alkaline	acid	acid	sl'ghly acid	alkaline	acid	sl'ghly acid	acid	sl'ghly acid	sl'ghly acid
Albumin	0	0	0	0	0	0	present	large am'nt	0	0
Indican	0	0	slight	very slight	slight	0	0	0	0	0
Urea	11.55	10.52	17.46	11.33	16.63	10.67	19.80	16.79	16.3	12.29
Uric acid	0.3445	0.221	0.272	0.205	0.3163	0.2841	0.1972	0.7210	0.428	0.40
Ratio $\frac{\text{urea}}{\text{uric acid}}$	34	48	64	55	53	37	100	23	38	31
H_2SO_4 preformed	0.8847	0.676	1.20	0.731	1.498	1.113	1.4476	1.199	1.26	0.98
H_2SO_4 combined	0.1146	0.127	0.224	0.192	0.2681	0.1158	0.1884	0.1935	0.316	0.193
Ratio $\frac{H_2SO_4\ p}{H_2SO_4\ c}$	7.7	5.3	5.4	3.8	5.6	9.6	7.69	6.2	4.0	5.1
Total N	5.4	4.92	8.15	5.30	7.771	4.985	9.251	7.832	7.73	5.74
N of NH_3 grms.	0.3967	0.155	0.266	0.15	0.3287	0.3632	0.7920	3.3716	6.35	0.66
N of NH_3 (per ct. of total N)	7.4	3.2	3.3	2.8	4.2	7.2	8.6	4.8	8.2	11.5

TABLE IV.—Continued.

	Case XI.	Case XII.	Case XIII.	Case XIV.	Case XV.	Case XVI.	Case XVII.	Case XVIII.	Case XIX.
Volume	650	840	950	950	1035	465	1500	1375	1400
Specific gravity	1018	1021	1014	1021	1014	1029	2018	1011	1008
Reaction	acid	acid	acid	acid	acid	alkaline	str'ngly acid	acid	slightly acid
Albumin	slight	0	0	0	0	0	0	0	faint trace
Indican	moderate	0	0	0	0	0	faint trace		
Urea	14.47	16.28	18.94	22.53	9.396	14.35	20.78	12.71	9.91
Uric acid	0.428	0.3326	0.2971	0.4639	0.2851	0.54	1.706	0.066	0.141
Ratio $\frac{\text{urea}}{\text{uric acid}}$	35	49	64	48	33	26.5	12	193	70
H_2SO_4 preformed	1.13	1.4175	1.602	1.6272	0.5555	0.849	1.4993	1.02	0.643
H_2SO_4 combined	0.166	0.2105	0.1470	0.1918	0.1584	0.170	0.2397	0.143	0.134
Ratio $\frac{H_2SO_4\ p}{H_2SO_4\ c}$	6.8	6.7	10.9	8.5	3.5	4.98	6.26	7.12	4.8
Total N	6.76	7.602	8.843	10.53	4.384	6.71	9.709	5.94	4.63
N of NH_3 grms.	0.35	0.5687	0.6824	6.6184	0.1625	0.235	0.7025	0.14	0.28
N of NH_3 (per ct. of total N)	5.2	7.5	7.7	5.9	3.7	3.5	7.2	2.28	6

In Case I. the aromatic sulphates were not increased, but indican was present in every specimen examined (Table V.):

TABLE V.

	Case I.								
	Oct. 26, 1899	Oct. 27, 1899	Oct. 28, 1899	Jan. 20, 1900	Feb. 14, 1900	April 4, 1900	May 14, 1900	May 14, 1901	May 16, 1901
Volume (c.c.)	1130	810	1175	1000	1000	1150	1850	1140	1575
Specific gravity	1023	1027	1024	1023	1029	1023	1016	1024	1019
Reaction	acid	acid	acid	acid	acid	acid	acid	acid	str'ngly acid
Albumin	0	0	0	0	0	0	0	0	0
Indican	moderate	moderate	moderate	strong	present	moderate	moderate	fairly strong	large am'nt
Urea	22.88	20.01	24.13	21.95	26.87	25.6	30.0	30.95	29.86
Urea acid	0.634	0.4512	5.541	0.505	0.648	0.688	0.850	9.932	0.8974
Ratio $\frac{\text{urea}}{\text{uric acid}}$	36.09	44.32	44.6	43.5	41.5	37.2	35.3	33.2	33.0
H_2SO_4 preformed	2.079	1.726	1.978	1.66	2.06	1.942	2.07	2.61	2.2748
H_2SO_4 combined	0.162	0.125	0.189	0.148	0.21	0.180	0.226	0.204	0.2622
Ratio $\frac{H_2SO_4\ p}{H_2SO_4\ c}$	12.8	13.8	10.4	11.2	9.8	10.8	9.16	12.8	8.68
Total N	10.69	9.35	11.27	10.25	12.56	11.96	14.02	14.46	13.95
N of NH_3 grms.	0.588	0.468	0.650	0.68	0.49	0.49	0.54	0.63	0.8158
N of NH_3 per ct. of total N	5.5	5.0	5.77	6.6	3.9	4.1	3.97	4.3	5.8

The amount of uric acid excreted showed no uniformity in the different specimens. In some cases uric acid was in excess, in others it was in less amount than normal. The average of all the specimens showed a ratio of uric acid to urea of 1:50, or a normal ratio. (See Tables IV. and V.)

In the graver forms of acid intoxication, as in diabetes and certain forms of mania, the acid excretion is in so large quantities that there is a marked increase in the ammonia excretion to neutralize this acid. In the cases of rheumatoid arthritis, however, the percentage of ammonia is not increased, so as to be an indication of a condition of acidosis. The normal percentage of the nitrogen of ammonia is from 2 to 5 per cent. of the total nitrogen. In only twelve of the specimens examined above does it exceed 6 per cent., the average being 5.4. (See Tables IV. and V.)

In reviewing the above records of patients with rheumatoid arthritis, it is found that in all cases with progressive lesions there are certain definite evidences in the urine of perverted metabolism. In only three cases were the stomach contents examined, and in all of these there was absence of free hydrochloric acid after a test meal, although the patients had no other symptoms of gastric indigestion. Intestinal putrefaction was found to be constantly excessive in those patients who had active symptoms of the disease. Besides these evidences of gastric and intestinal disorder there was regularly found in the urine organic acid other than that normally present. As the various forms of organic acid are readily oxidized in the body, the amount formed is probably in excess of the amount excreted.

Patients leading as inactive lives as those with rheumatoid arthritis would naturally be subject to gastrointestinal indigestion, but the regularity with which such symptoms are noted and their degree would suggest that certain of the disturbances of nutrition which occur in rheumatoid arthritis are due to these putrefactive processes in the intestine.

In conclusion, I wish to acknowledge my indebtedness to Dr. Herter in the carrying out of this work. The presence of acidosis in rheumatoid arthritis was first noted by him, and his records of cases are included in the above summary. I wish, also, to express my gratitude to those physicians who placed their patients under observation, especially to Dr. V. P. Gibney, Dr. A. Lambert, and Dr. C. A. Ransom.

THE DIAGNOSTIC VALUE OF LEUKOCYTOSIS.[1]

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The remarkably large fluctuation in the number of leukocytes circulating in the peripheral blood constitutes one of the most intensely interesting of hæmatological phenomena. The relationship

[1] Read before the Indiana State Medical Society, May, 1904.

of these changes to different morbid processes has been the subject of the most extensive clinical and experimental study, with the view, among other things, of establishing working, diagnostic, and prognostic formulæ. This, indeed, was done, but with more haste than discrimination, and without due regard to the anatomicophysiologic foundation upon which they ought to rest. Growing out of the resulting disappointment, and with a similar disregard of the fundamental facts above referred to, there has been in certain directions a distinct tendency to greatly depreciate or even reject the phenomena of leukocytosis as a substantial clinical aid. It must be admitted that the variations in the number of leukocytes show some extraordinarily bizarre tendencies which make it difficult or even impossible to formulate rigid and inflexible rules. This, however, is also true of the temperature and pulse curves, to which are nevertheless assigned a high value. A careful study of the phenomena of leukocytosis in its physiological and pathological relations will, I am fully convinced, lead to a similar conclusion with reference to the legitimate significance and value of variations in the leukocyte count.

While the purpose of this article is a purely clinical one with special reference to diagnosis, it seems advisable, for the reasons above given, to enter into a preliminary discussion necessarily in the barest outline of the data upon which leukocytic diagnosis rests.

Morphologically there can be recognized several different kinds of leukocytes, distinguished by marked characteristics, such as size of cell, size and shape of nucleus, and presence or absence of granules in the cytoplasm, and the tinctorial reactions of the different elements which go to make up the cell, especially when subjected to the action of aniline dyes.

For the purposes of this discussion the different forms of leukocytes may be briefly summarized as follows: First, the predominant type of cell known as the polynuclear neutrophile, which may be described as a spherical mass of protoplasm 7 to 12μ in diameter, the cytoplasm containing a greater or less number of rather small granules which are neither exclusively acidophile nor basophile, and are, therefore, called neutrophile; the nucleus is characterized by a peculiarly irregular form frequently made up of broken masses connected by fine filaments, the latter often being severed, thus resulting in several nuclei. Second, in numerical importance, the small lymphocyte, a cell from 6 to 9μ in diameter, the cytoplasm free from granules and containing a small round nucleus which nearly fills the entire cell. Third, the large lymphocyte, 10 to 15μ in diameter, with granules, not demonstrable by triacid and ordinary stains, but by the Nocht-Romansky method, and containing a single round or ovoid nucleus relatively small in comparison with the cell, and not staining deeply. Closely related to these morphologically are cells precisely like them excepting that

the nucleus is indented, and which are, therefore, called transitional forms, and the large mononuclear leukocyte. Fourth, the eosinophile cell, precisely like the polynuclear neutrophiles in every respect excepting that the granules in the cytoplasm are very much larger and have marked affinity for acid dyes, being, therefore, called acidophile, oxyphile, or eosinophile. Fifth, mast-cells varying greatly in size from 7 to 22μ, containing coarse granules which do not stain with either acid or neutral dyes, but with a special technique by basic dyes, hence called basophile. Sixth, and finally, a large cell 10 to 20μ in diameter, occurring in two forms (really two distinct cells), with either neutrophile or acidophile granules, and a single large round or oval nucleus and occurring in the blood only in diseased conditions, but normally present in the bone-marrow, the so-called myelocyte.

These different forms of cells are present in health in somewhat varying proportions, about as follows: polynuclear neutrophiles, 60 to 75 per cent.; small lymphocytes, 20 to 30 per cent.; large lymphocytes and transitional forms, 4 to 8 per cent.; eosinophiles, 0.5 to 5 per cent.; basophiles usually less than 0.5 per cent.

Concerning the biological character and relation of these different forms of cells, two opposing views are entertained: first, that of the Russian school, following the lead of Uski, which regards the lymphocyte as the youngest cell, and the other forms as representing evolutional changes incident to the age of the cell, in other words, that the neutrophile is an old lymphocyte; second, the view of Ehrlich, that the lymphocytes, neutrophiles, and eosinophiles have an independent origin and a complete autonomy of existence. The latter view is the one most generally accepted, and the only one which the writer believes to be supported by the facts. It is, moreover, vital to a correct interpretation of a differential leukocyte count, which should be made in substantially every case.

In the clinical study of the ordinary forms of leukocytosis, the lymphocytes, neutrophiles, and eosinophiles are the ones which principally concern us, too little being known about the mast-cells and other forms to assign them an important routine clinical role for the present at least. In regard to the three groups of cells above mentioned, everything appears to indicate that they have not only a separate origin with characteristic morphology and staining reactions, but that, as would naturally be expected, their functions are widely dissimilar in character. The neutrophile is the form of cell which is especially increased in the ordinary clinical forms of leukocytosis. By an increase is meant a larger number of these cells in a definite volume of peripheral blood than is normally present, the increase being brought about by various influences, some of which are understood, while others are not. The discovery of the phenomenon of positive and negative chemotaxis furnishes the key to the physiology and the clinical interpretation of this type of leukocytosis.

It is now well established by an overwhelming mass of clinical and experimental evidence that the introduction of certain chemical substances into the blood causes a rapid increase, perhaps usually preceded by a transient decrease in the number of these cells in the peripheral circulation. Among these are the toxins of certain organisms, such as the streptococci and the staphylococci; while others, such as those of the tubercle bacillus, bacillus typhosus, etc., either do not produce such an increase or may possibly have a diametrically opposite effect. In order that these chemotactic influences may be manifested it is necessary for the chemotactic substances to gain an entrance into the circulation—a point which is absolutely vital in the whole question of the diagnostic bearing of leukocytosis, and the neglect of which has led to much confusion. Especially is this true in its bearing upon the absence or presence of suppuration in some part of the body. This particular question is one of the most important and most frequent in this connection, and it is just here that the most conflicting observations have been recorded. In one of my own cases, for instance, an obscure subacute localized pulmonary lesion of some sort existed, the exact nature of which was in doubt, although the history rather pointed toward an abscess. Confirmation of this view was looked for in the leukocyte count, with entirely negative results. In the course of forty-eight hours after the patient entered the hospital the diagnosis was cleared up by the evacuation of an enormous pulmonary abscess into the bronchial tubes, which very nearly suffocated the patient, an excellent recovery following the spontaneous discharge of pus. It is very probable in this case that a thick, impervious, pyogenic, non-absorbing membrane had walled in the pus from the circulation, and had prevented the entrance into the circulation of the bacterial toxins which probably constitute the chemotactic substance in cases of suppuration. This same question must be kept in mind in the diagnosis of suppurative appendicitis, where perhaps more often than elsewhere the question of the existence or non-existence of a pyogenic process presents itself for solution. If the anatomical conditions are such that the toxins cannot to any great extent enter the circulation, a leukocytosis of diagnostic significance may be entirely absent. There is another feature, however, with which the diagnostician always has to deal, and that is the reactive or resistive power of the individual of which the leukocytosis is an expression. We must recognize in the occurrence of an active leukocytosis under such conditions the marshalling of the defensive machinery of the organism against an invading foe. If, now, the organism is overwhelmed by the intensity of the morbid process or from pre-existing disease, and lacks the ability to make an effective resistance, the leukocytosis will not appear. It also seems possible that peculiar idiosyncrasies may occur here as elsewhere.

Keeping in mind these conditions, the general proposition can

be made that the presence or absence of a suppurative process is indicated with considerable certainty by the presence or absence of a neutrophile leukocytosis, if other chemotactic influences can be eliminated; but, of course, like most diagnostic criteria, it must be weighed and checked by all the facts in the case.

The remarkably brief time intervening between the occurrence of the morbid excitation and the development of the leukocytosis precludes the possibility of an increase in the total number of leukocytes at all commensurate with the increase found in the peripheral circulation. The only other hypothesis and the one now generally accepted is that they are in large part stored in a quiescent state in some of the internal channels of the circulation and are suddenly called forth in response to the demand for their services on the part of the organism. It is believed by some that this storage is in the capillaries of the lungs, but Ehrlich does not hesitate to affirm that the bone-marrow is the only place where such a storage can be found.

There appears to be no doubt that the bone-marrow is the exclusive source of the neutrophile, its appearance there being first in the form of a so-called myelocyte or large mononuclear granulated cell, which, perhaps, never wanders outside of the bone-marrow into the general circulation except in morbid conditions and especially, though not exclusively, in myelogenous leukæmia. This view of the life-history of the neutrophile is established by a chain of evidence, clinical and experimental, which may be regarded as entirely conclusive and separates this cell and its progenitor, the neutrophile myelocyte, from all other forms of leukocytes by a sharply defined line of demarcation.

The eosinophile leukocyte, although not ranking next in numerical importance, will be considered here because of its close genetic relationship and morphological similarity to the neutrophile leukocyte. Owing to the resemblance just mentioned the eosinophile has been frequently regarded as a stage in the evolution of the neutrophile, and has been commonly spoken of as its senile form. This view is not in accordance with the facts, and it may be considered as proven that eosinophile leukocytes circulate in the blood as the progeny of the eosinophile myelocytes pre-existing in the bone-marrow. The behavior of the eosinophile under physiological and pathological conditions can only be explained on this hypothesis and presupposes radical specific differences in the nature and function of the two cells. The final proof of its completely independent existence as a separate cell form is furnished by the discovery of mytosis—a regenerative phenomenon—which is entirely incompatible with senescence. Moreover, under conditions which lead to an increase in the number of eosinophile cells in the peripheral circulation, marked changes have been noted (as, for example, by Opie,[1]

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, March, 1904.

in his recent article) in the bone-marrow, including among other things marked increase of mytosis among the cells above described as being the progenitors of the ordinary eosinophile leukocyte. Although perhaps not conclusively settled, it seems probable that like the neutrophile and unlike the lymphocyte, the eosinophile responds to certain chemotactic agents. Just what these influences are is known only in part, but the clinical association of eosinophilia with various forms of cutaneous disease, with trichina and intestinal parasites, gives to this blood phenomenon a highly important character. It is worth noting here that a parallelism exists between the behavior of the neutrophile and eosinophile leukocytes under chemotactic influences or at least a similarity in the respective vital conditions which produce or permit a large increase in the numbers of these respective cells. I refer to the reactionary power of the organism against invading infection. Opie has shown, for instance, that in guinea-pigs an intense and rapidly fatal infection with trichina causes a rapid diminution in the number of eosinophiles, while a mild or moderate infection with the same parasite leads to a more or less well-marked eosinophilia, thus indicating that the eosinophiles, like the neutrophiles, are rapidly increased, or at least thrown into the circulation from the bone-marrow in response to a demand on the part of the organism for their functional activities whatever they may be. The theory of Neusser, that their increase is incident to a sympathetic irritation, is not now generally accepted, although the facts upon which it is based are of great interest and certainly lend support to his views, or at least to a close relationship of eosinophilia to the sympathetic. Ehrlich believes that among other things the soluble products of broken-down epithelial cells have the power of exciting positive chemotactic influences upon the eosinophiles, leading to their local accumulation around the sites of ulceration and other destructive processes. An extended discussion of these questions is not within the scope of this paper, and I will for the present leave the eosinophile cell, having endeavored to emphasize two important facts: first, that this cell is specifically distinct and separate from all other cells in its genetic, biological, and functional relations; and, second, that experimental and clinical observation has shown that it responds in a peculiar manner to the influences of certain morbid agents.

With regard to the lymphocytes, their nature and origin are entirely different from that of the neutrophiles and eosinophiles. All the available evidence, experimental and clinical, points to the lymphatic apparatus as the source of these cells. It would be impossible to canvass this question fully within the scope of this paper, and only a few points can be mentioned. Clinically, an increase in their number is very constantly associated with disease of the lymphatic system, and the well-known tendency of tuberculosis and syphilis to implicate the lymphatic glands is the probable explanation of

the frequent occurrence of lymphocytosis in these two diseases. Possibly, also, in pertussis, another disease in which lymphocytosis is frequently noted, the explanation is found in an acute inflammatory swelling of the tracheobronchial lymphatic glands. It has further been observed that the blood which emerges from a lymphatic gland has more lymphocytes in it than when it entered—a fact which is only susceptible of explanation upon the ground of the formation of lymphocytes within the gland.

An effort has recently been made in several quarters to break down the sharp distinction heretofore supposed to exist between lymphatic and myelogenous leukæmia, and incidentally between neutrophiles and lymphocytes, especially because of the fact that in some of the cases of lymphatic leukæmia changes in the bone-marrow have been found. These facts do not appeaar to me to justify so sweeping a conclusion, and, indeed, they are not at all new, as Ehrlich a number of years ago recorded changes in the bone-marrow in lymphatic leukæmia and reported at least one case in which the bone-marrow was almost entirely converted into lymphoid tissue. Among the pathological facts pointing to a very sharp distinction between the nature and function of lymphocytes and neutrophiles may be mentioned the observations of Milroy and Malcolm, who found an increase of alloxur bodies in the urine in myelogenous leukæmia, but found no such increase in the lymphatic form. While much remains to be learned before the subject can be fully cleared up, it appears justifiable at present to regard the occurrence of a lymphocytosis as the clinical evidence of irritative lesions of the lymphatic system.

Keeping in mind, now, the biological facts above set forth in brief outline, and omitting for the sake of conciseness and clearness of conception of the main facts, certain subordinate or obscure points, such as the mast cells, the transitional forms, and the broad distinctions between the large and small lymphocytes indicated by the Nocht-Romansky method, we are ready to ask ourselves for more specific answers to the various questions concerning the significance of leukocytosis in general and the methods and precautions necessary for its proper interpretation. In a general way it may be said that there are two broad types of leukocytosis: one due to an irritative lesion of the lymphatic apparatus represented by a lymphocytosis, the other due to chemotactic influences and represented by a neutrophile or eosinophile leukocytosis, according to the specific form of chemotactic influences at work. This being the case, it is obviously necessary that not only the total number of leukocytes should be known, but the relative number of these three predominant types. This can only be determined by the dried specimen in the form of a thin film on cover-glass or slide properly fixed and stained in such a manner as to differentiate these various forms of leukocytes and determine the proportions of each present in a con-

siderable number of stained leukocytes, say, for instance, 500. For this purpose Ehrlich's triacid mixture, followed by methylene blue to accentuate the nuclei, is the best staining method, as it makes possible the differentiation of the different forms of granules leading to the recognition, among other things, of the myelocytes when present in the blood. The ordinary eosin hæmatoxylin method, which is more easily applied, enables us to recognize the three types of cells already referred to, with certain limitations of error perhaps too small to affect conclusions from a clinical point of view. By this latter method the neutrophile is recognized by the shape of its nucleus and the absence of visible granules, the eosinophile by its large, deeply stained granules, and its nucleus, which corresponds closely to that of the neutrophile, and the lymphocyte by its size, shape of nucleus, and absence of granules. With Ehrlich's stain, however, the neutrophile granules are distinctly visible, and this stain, supplemented when necessary by a special method for the mast-cells and the Nocht-Romansky method above referred to, is in every way to be preferred.

The essential point, however, is that in connection with every leukocyte count there should be a differential count of a properly fixed and stained specimen, with a view of determining the proportional number of the different forms present. In some cases it will be found that the increase is due almost entirely to lymphocytes, while in another it is the neutrophiles or the eosinophiles, or the increase may affect several types of cells at one and the same time, though it is nearly always the case that one or the other form of cell will be sufficiently increased to enable one to label the leukocytosis as belonging to a particular type.

In attempting to make an analytical study of my own experience I collated some seven hundred counts in a large variety of diseases, mostly of a chronic nutritional type, but find the task of their detailed study altogether too large for the scope of this paper, and have, therefore, selected 131 consecutive cases of chronic gastritis, with a view of studying the general character of these cases and determining what light, if any, the leukocyte count would throw upon the general features of a case. In substantially every case upon which the classification is based the leukocyte count was made during the progress of digestion. Furthermore, the cases are divided into six groups, the first comprising those of a leukocyte count with 1000 to 3000; the second, 3000 to 5000; the third, 5000 to 10,000; the fourth, 10,000 to 15,000; the fifth, 15,000 to 20,000, and the sixth, over 20,000. The method sometimes adopted of giving the average count in a particular type of disease is obviously absurd, and can lead to no rational conception of the meaning of leukocytosis and its character in that disease. As illustrating the force of this remark, I recall the report of a series of cases of pneumonia in which by the fallacy of averages, if the individual counts

were not examined, it would have been made to appear that the count in the cases which recovered was the same as in the fatal cases. In the fatal cases the count ranged from a very low count of perhaps three or four thousand in the cases which were overwhelmed by the infection and failed to offer any resistance to those of a very high count of twenty-five or thirty thousand, and it so happened that when these individual counts were added together and divided by the number of cases the result was almost precisely the same as the average in the milder cases.

It is only by dividing a considerable number of cases of particular diseases into groups based on the leukocyte count and studying these groups separately that any practical conclusions of value can be reached, or at least a rational attempt made to throw some light upon the question as to whether the number of leukocytes present in the peripheral blood has an important or substantial bearing upon the main clinical questions with which we are usually concerned.

So far as this particular series of cases is concerned the following tabular statement gives the result of such an analysis:

LEUKOCYTES IN 131 CONSECUTIVE CASES OF CHRONIC GASTRITIS.

Leukocytes	1000 to 3000	3000 to 5000	5000 to 10,000	10,000 to 15,000	15,000 to 20,000	Over 20,000
Cases	10	17	70	27	5	2
Per cent.	7	13	53	21	4	1½

In considering the leukocyte count in these cases it should be stated that in a large number of them, especially the earlier cases, no differential count was made. The only inferences, therefore, that can be drawn are as to the total number of leukocytes, considering the number of leukocytes to be of normal proportions so far as the different types are concerned. While this lessens their value and is a defect which should be remedied in all further work along these lines, yet it is undoubtedly true that a very large proportion of all cases of leukocytosis is of the type just indicated, or, rather, that the increase affects the neutrophiles more than any other form of cell. Any conclusion, therefore, that can be based upon such a study would not be greatly invalidated.

In carefully studying the groups of cases of gastritis made with reference to the leukocyte count, I have been unable in the first three groups ranging from one to ten thousand to discover any striking characteristics belonging to each one. Their response to therapeutic measures and the general severity of the morbid process were very much the same in one group as in that of another, excepting that in the first group in which the leukocyte count ranged from

one to three thousand there appeared to be a somewhat severer grade of general debility and lack of vitality than in the other two. This, however, was not very marked, and the number of cases was somewhat too small to base a definite conclusion upon them in this respect. Moreover, these features of individual cases were more accentuated in some of the patients with higher leukocyte counts than in those with lower. Ehrlich himself, I believe, does not attach great importance to the condition known as leukopenia, and further observations will be required to settle this point.

When it comes, however, to the cases with counts ranging from ten to fifteen thousand there is in a large proportion of them strong evidence of the sort of infection which is commonly designated autointoxication of gastrointestinal origin, and I am of the opinion that leukocyte counts of this range have some diagnostic significance in this direction. With reference to the cases with a count of from fifteen to twenty thousand, this is still more marked. The two cases with counts above twenty thousand were complicated, one with tuberculosis with a mixed infection, and the other with a chronic infection of unknown nature, which proved fatal, no opportunity being given for an adequate study of the case.

There are many other questions concerning leukocytosis which it was my intention to canvass in this paper, but the proportions which it has already assumed make it necessary to close at this point.

The following conclusions appear to me warranted at the present time:

1. A routine enumeration of the white cells in the peripheral blood is of sufficient importance to be made a regular procedure so far as possible in all cases.

2. A single leukocyte count is entirely insufficient as a basis of conclusion in any given case, and should be followed up by several made under different conditions.

3. An increase beyond ten or twelve thousand leukocytes in the peripheral blood indicates varying grades of intoxication, with chemotactic substances of some sort or another.

4. Whether it indicates suppuration or not is a question to be determined by carefully weighing all the facts in each case.

5. The leukocytes indicating suppurative and allied processes are of the neutrophile type.

6. The eosinophile form of leukocytosis indicates among other things, and perhaps principally, cutaneous or parasitical diseases in the intestine or elsewhere.

7. Lymphocytosis clinically signifies an irritative lesion of the lymphatic apparatus.

8. A differential count should be made in all cases to determine the type of cell which has been the subject of the principal increase where such increase exists, and such records carefully kept and

collated as a basis for the determination of the clinical significance of leukocytosis in the future.

9. In the diagnosis of malignant disease a leukocytosis is of very subordinate value, and when present is probably not due to the malignant disease, *per se*, but to coexisting chemotactic toxins.

THE PRESENCE OF AIR IN THE VEINS AS A CAUSE OF DEATH.

By James S. Greene, M.D.,
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Ever since my graduation thesis was published under the above title[1] in 1864 I have thought that some time I might prepare a supplementary paper. The present article is an attempt to put the thought into execution. While scientists and observers have had their periods of productive activity, it seems to be time for the mere chronicler and commentator to take up his task. In attempting this in supplemental form I shall hope to escape the charge of egotism if in the one paper I sometimes refer to the other and quote a passage here and there.

Forty years ago the subject had been slumbering for a quarter of a century. The preceding period of active interest had culminated in the vote of thanks to Amussat at the close of the discussion which followed the report of Bouillaud[2] to the French Academy of Medicine.

The practical result of this long academic dispute was, as well expressed by Couty, "to make the entrance of air a classical question;" all surgeons knew the danger of certain cervicothoracic venous wounds and the number of cases in operations rapidly diminished. Besides the case of Barlow,[3] omitted from my earliest list, a fatal case was reported by Trélat[4], and like accidents with recovery are recorded by Armsby,[5] Cheever,[6] Tadlock,[7] and Courvoisier.[8] At the present day surgeons, without ignoring or belittling, have practically eliminated the danger in operations within the recognized danger space. They proceed though they hear the warning sound, but they put on instant pressure at the proximal end of the wound. Of course they avoid the conditions which may invite trouble.[9]

When I wrote a new-found variety of the accident was coming into view, and I aimed at a re-awakening of interest. Cases of death by the entrance of air through the uterine veins were then little known, and there was again, as in the days before Amussat, much skepticism. Years followed, during which general assent prevailed regarding the actual dangers of the accident; and the

acknowledged danger region, already including the uterine veins, had also come to include the sinuses of the dura mater.[10] History still repeats itself. Within the last ten or fifteen years skepticism again has found expression; but while the earlier doubts had their excuse in paucity of recorded facts, the later ones are in some measure due to the overlaying of facts upon facts, with resulting confusion of inference.

In the earlier paper I gathered notes of 11 cases attributed to spontaneous entrance of air into the uterine veins, and 4 cases of forcible injection of air into the uterus. With these were brought into comparison an analogous class "in which gas seems to be developed within the vessels instead of admitted from without." "In fact," I wrote, "there appears to be a regular gradation of instances from such as are physiological to such as are clearly due to the operation of physical laws." After citing instances I added: "It is impossible not to associate this class of cases with that immediately under discussion; and we must admit the possibility of some peculiar and unfrequent condition of the system which predisposes to the reception of the noxious agent or to the more rapid development of fatal effects." And quoting further: "In those cases where gas is unquestionably developed within the vessels it would be useful to investigate its exact composition, and thus determine whether it is generated by decomposition of the blood or merely set free from solution;" added, "the gas might be collected in an inverted beaker and measured approximately, and in a case admitting of doubt whether the gas was atmospheric air or not the rough analysis resorted to by Roux would suffice." Now it is singular and noteworthy that no chemical analyses of gas found in the heart or vessels have since been recorded with one exception to which I shall refer later.

In 1863 Pasteur,[11] then just elected a member of the French Academy of Sciences, received the unanimous award of its *Prix de Concours* for his "memoir upon the organized corpuscles existing in the atmosphere," a memoir which gave the *coup de grace* to the theory of spontaneous generation. From this epoch-making discovery have developed the stupendous and ever-extending achievements of modern bacteriology.

Now let us leap the intervening forty years and ask what is the present attitude of bacteriology toward the venerable subject of Air in the Veins. Professor Welch[12] tells us that to *gas sepsis* "belong most of the cases which have been reported as deaths due to the entrance of air into the uterine veins." "No case of alleged air embolism from the uterus," he says further, "however plausible, can be considered as positively proven without a satisfactory bacteriological examination."

This opinion is founded on the fact that bacillus aërogenes capsulatus has been discovered in cases of uterine infection where gas

has been found in the tissues and vessels after death. Dr. Welch states that "the limitation of gas to the right heart and adjacent vessels may occur from invasion of the gas bacillus, and is not, as is often represented, peculiar to air embolism." He does not cite any cases illustrative of this statement, and we may accept the fact on his high authority; but it would, nevertheless, be extremely interesting to read the clinical history and the minute post-mortem conditions found in such a case. It must be conceded, as was regretfully conceded forty years ago, that published cases are often sadly inadequate and inconclusive, and we may sympathize with Dr. Welch in the lament that: "Did we not know how long it takes new knowledge . . . to penetrate throughout the medical world it would be amazing that cases should still continue to be reported . . . of deaths ascribed to air embolism without any bacteriological examination, or even any reference to the possibility of any other explanation."

I cannot forbear to ask, however, if the fervor of the scientist and discoverer has not led him to some overemphasis in statement? I write not from a bacteriological point of view, but, as I have said, only from the historical and clinical viewpoint; but I cannot forget how much the earlier views of bacteriologists have been modified with regard to the virulence of diphtheria bacilli.

The earlier doctrine was that the presence in the throat and nose of the Klebs-Loeffler bacilli was adequate evidence of the presence of the disease in the individual, and of danger of contagion from him; but in April, 1902, a committee of the Massachusetts Association of Boards of Health[13] made a report to that body on Diphtheria Bacilli in Well Persons. I quote from that report this paragraph: "We seem to be justified in concluding, from an examination of the experimental and clinical evidence at hand, that only a small percentage of the morphologically typical diphtheria bacilli found in well persons not recently exposed to the disease are virulent." And again: "They (the virulence tests) bring out the fact that if a healthy person is found to have Klebs-Loeffler bacilli, and there is no connection traceable between that person and cases of diphtheria, the chances are very much in favor of the bacilli being non-virulent."

To-day, according to Solomon,[14] bacteriologists are as far as ever from agreement as to the classification and identification of true and false diphtheria bacilli.

Now may not the bacteriologist hereafter modify his present view regarding the gas bacillus, which is, that its presence in blood-vessels or tissues, even though demonstrated unnumbered days after death, *must* set aside a presumption of air entrance as the cause of death[12] in a case which clinically belongs in that category? And even though he concede nothing, has the bacteriologist the final word? Suppose the pathological chemist should sustain the

obstetrician who makes claim that a given case of sudden death after childbirth is due to the entrance of air into the uterine veins, and should, by analysis of the collected gas, affirm that it was atmospheric air, would not the tables be turned, and would not the burden of proof rest upon the scientist who asserts that the presence of gas bacilli found in tissues after death controverts the theory of air embolism as the cause of death in the case? I believe that bacteriologists know that the gas formed in tissues during life or after death by the agency alike of aërobic and anaërobic bacilli is a compound of hydrogen and carbon dioxide; but I do not think that they have published this knowledge to the world. They also suppose that this gas mixture or compound is a result of fermentation of sugar formed by decomposition of proteids or carbohydrates in the system, or of sugar already present in the blood (in case of diabetics), through the agency of some one or more varieties of gas-producing bacilli.

In the mean time there is the fact recorded by Jürgensen,[49] that Hüfner analyzed the gas collected from abscesses behind sterno-clavicular articulation and from the upper part of the thigh, and found nitrogen, 84.45 parts; oxygen, 14.05 parts; carbonic and sulphurous gases, 1.05 parts; but whether the gas was developed in the abscesses or found its way thither from without, both in this case and in that of an analysis by Dressler, there was doubt.

It is nearly ten years since the discovery of the bacillus aërogenes capsulatus, the agency of which is invoked to discredit the great mass of evidence accumulated in medical literature showing the danger of air entrance through the uterine veins, and is it "anything less than amazing" that we have to go back to the time of Roux[15] in the early years of the last century to find more than one recorded statement of measurement or analysis of gas found post-mortem in the heart or vessels?

Now let us examine the single observation to which I have alluded. It is not the observation of a bacteriologist. Indeed, it was published when bacteriology was barely emerging from its chrysalis state. Moreover, it is an observation which supports neither the doctrine of the demonstrators of gas sepsis, nor that of the advocates of air embolism, but illustrates that conjectural *terra incognita* or possible middle ground between the territories, equally definite, as I must maintain, of gas sepsis due to bacilli and of air embolism. It seems an instance fairly demonstrated of gas set free from solution in the blood. The case is recorded by M. Hervieux.[16] A young woman was delivered of her second child, a male, after normal labor. On the tenth day a vaginal injection was administered for the correction of fetid lochia. Careful precautions were taken against the admission of air. The eleventh day another injection was given, with the same precautions. This second injection at 7.30 P.M. was followed by the loss of 750 grams of fluid

blood, and by a rigor and chattering of teeth. Later in the evening she had an angry quarrel, ending with an ungovernable nervous crisis. Death half an hour after midnight.

Autopsy was made thirty hours after death. There was no evidence of putrefaction. Cardiac vessels were carefully tied. Heart distended with gas; vena cava the same; contents of latter lost by accidental puncture, but whole inferior cava from right auricle to primary iliacs full of frothy blood. None in iliacs nor utero-ovarian veins, nor superior cava nor its tributaries. Uterus showed no vestige of inflammation nor suppuration. Washing of the interior at fundus revealed the seat of the hemorrhage: two little erosions the size of a pinhead, with small red clots adhering. Appendages perfectly healthy. Gas from heart, chiefly from right cavity, but some from left, collected under water to a volume equalling 40 to 45 grams of water, analyzed with the following result: oxygen, 7 parts; carbonic acid, 11 parts; nitrogen, 82 parts. Same gases as those of air, but in different proportions.

M. Hervieux cites M. Durand-Fardel's case reported at the Academy of Medicine, session of December 9, 1851. A lady aged fifty-six years, of healthy appearance, in coming out of a bath felt oppressed, sank in a chair without power to speak, and died in five minutes. At the autopsy, twenty-two hours after death, the heart was found to be much distended and to contain bubbles of gas, with very frothy blood. The whole abdominal venous system was engorged with dark, frothy blood, and the blood of the splenic and portal veins contained numerous bubbles of gas.

M. Durand-Fardel adopted the view of a spontaneous exhalation of gas during life in the venous system, probably due to an unknown alteration of the blood.

The analogue of these and similar observations is found in the caisson illness. It seems to be determined that symptoms and lesions in that disease are due to the presence in the system of gas withdrawn from solution in the blood.[17]

Hervieux's case was not one which would to-day be claimed as one of air embolism, but rather as an instance of gas sepsis. Its long interval of ten days after delivery, and its interrupted progress toward the fatal issue would remove it from the former category and align it with the latter. The advocates of gas sepsis might claim it as their own but for the counterevidence of the gas analysis.

The puerperal cases on which Professor Welch relies for the support of his contention are all cases of emphysema of uterine walls, and in all but one there was physometra. Such cases develop slowly, either days after delivery or incidentally to the presence in the uterus of a decomposing fœtus. They form clinically a class by themselves. The reasonable inference in these cases is that the bacillus aërogenes capsulatus found *post-mortem* in the tissues is the fatally noxious agent; but the weak point in the demonstra-

tion is the omission to collect and analyze the gas found in the vessels. When death has occurred suddenly, after hours or days of localized emphysema, the event may well be suspected to be due to distention of the right heart or invasion of the pulmonary capillaries by the gas after long overdistention of neighboring or remoter tissues.

Cases of injury or operation with complications such as gangrene and emphysema are recorded in which slow or sudden death has ensued, and the veins and heart after death have been found to contain frothy blood.

They form a class wherein the presumption now is that the gas found post-mortem is the product of sepsis. Whether the presence of this gas in the heart and pulmonary vessels be the proximate cause of death is a question which should be decided in each instance by the clinical history and the quantity and distribution of the gas.

Many cases of this character were recorded before the discovery of gas bacilli, and attributed by the observer to slow or rapid admission of atmospheric air.[18] Of these only one (referred to by Dr. Porter) is found in surgical history of modern war.[19]

It is curious to note that notwithstanding Baron Larrey's[20] well-known remark concerning the frequency of deaths on the battlefield from entrance of air into the veins, neither the index of the "Surgical History of the War of the Rebellion" nor that of the Chino-Japanese War contain any reference to air embolism.

Parise[21] affirms that the putrid character of the gas developed in some cases of gangrene determines no septic action, but produces death in the same way as does air accidentally entering the veins.

Professor Welch himself admits the "possibility that gas generated by bacteria may have entered wounded veins in sufficient amount and so suddenly as to have caused death."

The surprising thing is that this theory of gas sepsis should be invoked to invalidate a well-established presumption of death by air entrance in a class of cases wholly unlike these septic cases in their clinical aspect, and this without a single supporting verification by gas analysis. On the other hand the clinical picture of spontaneous air entrance through the uterine veins is identical in feature with the same accident occurring in surgical cases and in attempts at abortion. It occurs at the time of delivery or shortly afterward, is sudden, and is seldom lacking in some of the characteristic symptoms.

Take, for instance, the case of Cordwent.[22] A healthy young woman of twenty-eight. Babe and placenta expelled while the patient was standing. Babe fell to the floor, dragging out the placenta. Almost immediately a kind of gurgling sound was heard. Patient remained standing about a minute, holding on to the bedpost, and then exclaimed: "I cannot see; I feel faint; lay me on the bed." This was done, and she died instantly. Autopsy

twenty-four hours after death. Uterus healthy. A portion of wall of fundus about the size of a five-shilling piece, slightly more puffy than the other portions; and on cutting into it air-bubbles escaped. There was no laceration of placental surface. The uterine cavity contained only one small clot; its lining membrane was healthy.

The coronary vein of the stomach was distended by air, and contained only a fine thread of blood. The right side of heart was slightly gorged, and when the auricle was punctured air-bubbles escaped from its contained blood. There can be no mystery about the mechanism of this fatal event. The uterus relaxed after the pain which caused the rapid expulsion of the child, and produced a partial vacuum. The inrushing air at the moment when the placenta passed through the vaginal outlet found entrance into the venous system through uterine sinuses not wholly closed by coagula. The inlet was sealed by collapse of the vaginal walls and perhaps by a clot, and the ascent of the imprisoned air to the heart was favored by the erect position of the patient.

Other cases have been reported by Heckford,[23] Davidson,[24] and Braun.[25] Lauffs[26] gathered notes of 18 cases which he classified as cases of spontaneous air embolism through the veins of the uterus. Nine of them I have in this or the earlier paper cited from the original sources. Two others, reported by Draper,[33] occurred in the offices of abortionists, and may have been forced rather than spontaneous, while three, observed in the clinic and polyclinic of Bonn[18] and elaborately reported, were cases of artificial delivery in which it would be difficult to exclude the possible agency of shock or sepsis or both as contributing to the fatal results, though air was found at the autopsy in the right heart and in the large veins in each case. There remain the four following cases to be credited to Lauffs: Levy[27] reported a case of a woman of fifty years who died while undergoing a delivery by forceps. At the autopsy were found partial loosening of the placenta, frothy blood in abdominal veins, air in right internal spermatic vein and in pulmonary vessels. Fürst[28] reported a fatal case occurring in a Vienna hospital. A woman aged twenty-five years, secundipara, who on expulsion of the infant was turned from side to back. Thereupon she immediately became asphyxiated, lost consciousness, and died in an hour after delivery. The autopsy revealed air embolism as the cause of death.

Bischoff[29] gave a case recorded by Hegar. A woman who had experienced a normal labor died suddenly on the fifth day of lying-in. She had laughed loudly while engaged in conversation, and immediately convulsive movements and rattling in throat ushered in death. Autopsy showed frothy blood in right ventricle and right branch of pulmonary artery. Air escaped from veins of the dura. These three cases, while suggestive of nothing so much as spontaneous air embolism, are too meagre of detail to permit of exact

conclusions. The fourth, which I condense in extracting from the paper of Lauffs, is a well-observed case of Kezmarsky[30] occurring at the University Lying-in Clinic of Budapest, March 19, 1877.

An unmarried washerwoman of thirty years was admitted at 10 A.M. in labor at full term of her fourth infant. Hydramnios was diagnosed. From noon the pains, which had been few and weak, became frequent and stronger. About 3 P.M. a bag of membranes emerged, the size of a fist, and during the momentary absence of the midwife from the bedside, burst, flooding the bed with the waters. About fifteen minutes afterward, while the woman was still clearing up the water, the patient suddenly jerked her head backward, gasped painfully for air, her face became livid, and her breathing stopped. The whole scene passed with such lightning quickness that the assistant, Dr. Liebmann, who reached the bed in two minutes, found no pulse, but noticed two incomplete respiratory movements of the thorax, and heard the heart's action faintly as the patient lay on her back. While artificial respiration was undertaken, Dr. Liebmann applied forceps to the child's head in the pelvis, and delivered an asphyxiated male infant of 2780 grams' weight. External pressure caused the expulsion of the placenta directly afterward. In spite of all efforts the heart's action ceased and the patient expired. The liquor amnii amounted to 4 litres. At first glance Dr. Liebmann had the impression that eclampsia might have occurred, but in contradiction of that idea came the decided assurance of the practitioner present and the experienced midwife, that there were no convulsions. The belief was then adopted that either pulmonary embolism or the entrance of air into the veins was the cause of death. Autopsy twenty hours after death by Professor Scheuthauer. The heart was moderately contracted. The left ventricle contained a little fluid blood of yellowish-white color. In the right ventricle, especially near the pulmonary valves, also in the inferior cava and the uterine veins, was pale reddish-brown fluid blood mingled with small and large air-bubbles. Frothy blood flowed from the veins of the uterus when that organ was incised and pressure applied. Professor Scheuthauer thought that the air present was not the product of putrefaction, because the body presented no signs of decomposition, and there was no trace of air found in the jugulars nor the other large vessels.

Kesmarsky remarks concerning this case that the manner of entrance of air was obvious. At the rupture of the membranes the woman was nearly in the Sims position, for she lay on her left side with thighs drawn up, pelvis oblique over the bed, and head on the edge of two flat hair bolsters, so that the face and thorax seemed a little downward. The prominent abdomen was lower than the pelvis, and noticeably lower than the *ostium vaginæ*. The mechanism of the accident was as follows: When the large bag of membranes was suddenly extruded and ruptured, a space was made

between the collapsed membranes and the flabby, voluminous walls of the multiparous vagina. At the same time the intra-abdominal pressure, by the quick escape of a very large quantity of amniotic fluid, became negative, and air rushed in between the membranes and the walls of the uterine cavity. The fetal head descended and the retracting cervix uteri closed around it. The placenta, having become partially detached by the contracting and relaxing uterus, left openings into uterine sinuses through which the air, imprisoned in the uterus, directly entered the veins. All this occurred within the five minutes which elapsed between the bursting of the membranes and the first symptoms of difficult breathing. The absence of external hemorrhage has no value as opposition testimony, because such blood as issued from the placental sinuses was, like the air, prevented from escape by the presence and pressure, as a tampon, of the fetal head.

As though to furnish more links to the chain of proof, surgical cases are not wanting with post-mortem demonstration of fatal air entrance by way of the uterine veins. Wyman[31] and Cheever[6] have each reported a case occurring during aspiration of pelvic tumors. Several instances of sudden death in cases of placenta prævia have been recorded and discussed in German periodicals, and are reasonably ascribed to air embolism. To this category belong cases of Kramer, Kruckenberg, and Heuck.[32] But when in such cases, those for example of Lesse and Zorn,[32] death has been much delayed, the door of controversy is opened as to the possible agency of gas sepsis. The eight cases which I have chosen for citation, added to the eleven collected in my thesis, all lack, it is true, the ultimate proof of the chemical analysis, while some are extremely meagre; but all the reported cases of supposed gas sepsis are likewise unsupported by chemical proof. If the latter class stands on a bacteriological basis, surely the former may claim an equally firm foundation on clinical grounds and convincing analogies.

I suppose that most practitioners of long experience have witnessed cases of sudden death after childbirth, with attendant symptoms indicating the possible entrance of air into the circulation, but have been unable to verify this inference by means of an autopsy.

It is probable that more fatal cases of air entrance through the uterine veins occur than do like accidents in surgical operations, and that present-day obstetricians are less generally cognizant of this danger than surgeons. There would be a correlation between these two facts, if facts they be.

Skeptics have adduced the fact that the accident has not occurred in Cæsarean section. The reply is that since atmospheric pressure does not become negative, conditions promoting the accident are not afforded in that operation. According to Cohnheim, air can find entrance into the veins whenever atmospheric air has access

to the cavity whose tension is less than that of the air. These conditions may be fulfilled in particular cases in a variety of ways:

Veins and sinuses may be emptied by hemorrhage and remain patulous; violent nervous agitations may induce succussion of abdominal walls so as greatly to extend the area of *l'espace dangereuse;* a contracting and relaxing uterus may act as a receiver and pump; or a sudden turning of the body may cause retreat of the viscera, and suction of air through a relaxed and patulous uterus and vagina. Air once introduced may be hindered from escape through the channel of entrance, and the greater veins may easily be the path of least resistance. None of these conditions are presented in the operation of Cæsarean section.

As the controversy stands to-day, in the light of the solitary gas analysis of Hervieux, it would seem reasonable to maintain that no case of assumed death by gas sepsis even with gas bacilli demonstrated could be declared proven, nor any case of assumed death by air embolism could be declared spurious or disproven without collection of the gas found in the heart or vessels, and the demonstration of a pale-blue hydrogen flame on ignition, or an explosion due to the presence of hydrogen or marsh gas.

True, the recorded cases of spontaneous uterine air entrance are rare. So, too, are those of pulmonary embolism after childbirth; and it may be, as has been affirmed, difficult or impossible to distinguish between these two accidents by the symptoms. Pulmonary embolism, however, is usually consequent upon phlebitis and thrombosis of the thigh, and occurs with these concomitants days after delivery, as gas sepsis does with the surroundings of gangrene or decomposition; while spontaneous air embolism, as has been shown, is attendant upon, or follows shortly after, delivery. All these accidents indubitably sometimes occur, and in the interest of scientific truth what is most needed is the urging upon all observers the careful reporting of cases, and the determination in each case of the exact nature of the accident, whenever possible, by post-mortem investigation carried to its last analysis.

The literature of alleged forcible introduction of air into the veins of the uterus has expanded in forty years from the four cases contained in my thesis to a large number.[33]

To the present inquiry these cases have pertinence, first, because, taken as a whole, the cause of death, when confirmed by the finding of air in the right heart and large veins, does not admit of dispute; second, by reason of the striking similarity in symptoms between them and those cases which are chiefly depended upon as characteristic instances of fatal spontaneous air entrance, whether surgical or obstetrical; and it might be added, third, because they offer, especially when the medico-legal element is introduced by a charge of criminality, the best prospect of determining the minimum quantity of air necessary to produce death when admitted into the

veins of the human body. This brings up the third ground of that skepticism to which I alluded to in my opening paragraph, and I shall refer to it later.

Upon the mechanical conditions concerned in the accident, nothing need be added to the remarks already made. Regarding proximate causes it is otherwise, for the period which this résumé is intended to cover is prolific in careful scientific search. It is impossible within the limits here permitted to do more than glance at the conclusions of a few among the noted men who have made patient study of the subject.

In voluminous literature the decade of the 70's, following the revival of professional interest, was surpassed only by the decade of the 30's; in systematic, scientific study and painstaking analysis it surpassed the 30's or any intervening decade, and the impetus thereby given to productive research has extended through the 80's and 90's to the present.

Doubtless both the interest and the results were enhanced by the introduction and the use of instruments of precision unknown to the former generation of workers, and by means of which conclusions could be made much more exact. Panum,[34] in Germany, and Oré,[35] in France, were among the last of the men of note who made contributions to the doctrine of air embolism before the new era opened.

Oré, in 1863, held that air not only distends the right cavities, but also has a sedative action upon the muscular fibre which determines paralysis of the right ventricle, herein taking similar ground to Busse[36] and Marchal (de Calvi).[37]

This chemical theory of Oré, which had some acceptance in France, was contradicted by the studies of Demarquay,[38] who, with his pupil Meric, concluded that air acts only mechanically, herein following the teaching of Magendie.

The theory of Boerhaave and later of Poiseuille,[39] that the lungs are the seat of circulatory obstruction, sustained by Ericcson and Milne-Edwards, was adopted by Claude Bernard[40] in 1873. Muron and Laborde,[41] working together in 1874, maintained the view that brusque injection causes death by distention of the right heart, while injection more slow determines death by suspension of the cerebral functions favored by the diminution of strength of the cardiac contractions. Kowalewsky and Wyssolsky,[42] of Kasan, in 1874, deduced from experiments on cats and dogs a belief in anæmia of the aortic system by the mechanical hindrance of froth in the right heart. Other essayists in the same decade were Pallas[43] and Esleben.[44]

In 1875 a young knight entered the lists to dispute the old doctrines and to establish a new one.

Louis Couty,[45] working in Vulpian's laboratory, made many experiments on animals, together with careful analysis and com-

parison of the labors and theories of all his predecessors in this field, and of all known cases of the accident. On this basis he developed in his thesis for the doctorate in medicine the theory which until recently has held the more general acceptance.

He denied the theories of cardiac paralysis, both chemical and mechanical; likewise the theories that air kills by reaching the brain or by obstructing the lung capillaries. He affirmed, and claimed to have proved, that the entrance of air produces one sole trouble, fall of tension and circulatory arrest; and that all general consecutive accidents, momentary, grave, or mortal, are the direct consequence of this initial circulatory trouble. This stasis of circulation is due not to paralysis of the cardiac walls, for they contract more energetically, but because they contract upon an elastic fluid (air) and compress it instead of propelling it. Further, the distention of the cavities causes tricuspid insufficiency and venous reflux. The blood current into the pulmonary arteries is checked with resulting cerebral anæmia, followed by bulbar death. M. Couty pursued his argument with such eloquence and elaborated it with such wealth of illustration and thoroughness of analysis as to captivate the reader and silence opposition. His doctrine received the seal of Cohnheim's[46] approval, and held undisputed sway for years.

Heart death was the accepted belief of V. Feltz,[47] 1878; Passet,[48] 1886; Jürgensen,[49] 1887. In this country Dr. Nicholas Senn,[50] in 1885, made a monumental study of the subject. He returns to the belief of some of the earlier writers, and espoused by Dr. John Reid, that the conditions producing death are (using Senn's language), "*a*, mechanical overdistention of the right ventricle of the heart and paralysis in diastole; *b*, asphyxia from obstruction to the pulmonary circulation consequent upon embolism of the pulmonary artery."

He believes, further, that "such air embolism is relieved in a comparatively short time provided the contraction of the right ventricle continues unimpaired for a sufficient length of time to force the air through the pulmonary capillaries into the general circulation."

Dr. H. A. Hare, of Philadelphia, in 1889, on the basis of research among the earlier writers and experiments of his own on dogs, avowed his belief in the harmlessness of air entrance into the veins of human beings during surgical procedures. He thought obstetrical cases presented different conditions and might have possibilities of danger.

To give his position its full advantage, I quote the following remark of Dr. Hare, though I have failed to find the paragraphs in his paper devoted to the alleged proof: "We have proved that the quantity of air entering the veins under such circumstances (surgical accidents) cannot be of any great quantity."

Dr. Hare thinks that "there is no evidence whatever that air may not be taken anywhere that blood can flow." But Poiseuille, 1837, is among those earlier authorities with whom Dr. Hare is familiar, and of him Couty remarks: "Le fait (est) bien prouvé par Poiseuille le sang spumeux necessite pour traverser un resean capillaire une pression plus forte que du sang pur." (Thèse, p. 35.)

Velpeau did not attack the proposition that the entrance of air into the veins had been the cause of fatal accidents, as Dr. Hare supposes, but took the true scientific attitude toward the subject, and by analysis of the reported cases, including one of his own, pointed out those which he classed as doubtful, others as probable, and still others as almost certain, not carrying any doubt to his mind. Had Dr. Hare in this spirit examined the record of some cases since Velpeau's time—Volkmann's case, surgery of the head; Trélat's, submaxillary; or Cheever's pelvic case—he must have modified, might have reversed, his opinion.

After these men of the 80's the pendulum of opinion begins to swing away from heart death, though so recently as 1902 we have an American writer, Dr. Malcolm Goodridge,[52] whose research and experiments lead him to the belief that death is due to one of two possible causes:

1. Gaseous distention of right auricle and failure of the blood to reach the left ventricle, and consequently anæmia of the brain centres.

2. And to his mind the more important factor, plugging of the coronary vessels with air emboli.

Hauer,[53] in 1890, holds to the theory of lung death, and with him stands the latest investigator, Dr. L. Wolffs,[54] of Berlin, in 1903.

Dr. Wolffs undertook a series of experiments on dogs to determine what becomes of air injected into the circulation, and what is the cause of death; and his conclusions are noteworthy. He finds that the air entering the venous system presses toward the heart. From the heart the pulmonary arteries are filled with air, which passes on into the capillaries. Here its progress meets with a very important resistance. The heart can overcome this resistance if too great a number of capillaries are not too suddenly obstructed. The heart will meet the increased demand the more easily the greater its strength and the less the amount of blood which has been lost.

On account of the peculiar anatomical relations which exist for the lung capillaries, the air is not pressed into the corresponding capillary system, but into the alveoli, where it mixes with the inspired air of the breath. It is not strange that in this process of filtration isolated air-bubbles find their way into the venous capillaries of the lung. This would again be a cause of death through embolizing of vital tracts in the brain, spinal marrow, or coronary arteries, an outcome surely rare, but one that could not be characterized as lung death.

What becomes of the large quantities of air injected, since it does not enter the general circulation nor remain long in the right heart and large veins, except in cases where the whole pulmonary tract is embolized by too large and sudden injections? Even subtracting absorbed oxygen the remaining amount is still far below the injected quantity. This can only be passed out through the lungs. If the explanation be not accepted that embolized pulmonary capillaries are the seat of interruption of the circulation, how could be explained the greater tolerance in cases of interrupted and renewed introduction of air?

Dr. Wolffs has never been able to find air in appreciable quantities beyond the pulmonary capillaries, neither in the left heart nor in the pulmonary veins, and thinks that only an open *foramen ovale* would permit the passage of air into the great circulation after venous injection. Recorded instances of such transmission he believes to be mistakes in observation due either to decomposition, gas formation *in vivo*, or entrance of air during section.

In all this maze of experiment and inference, always incomplete and often contradictory, is there any clue by which to arrive in sight of a goal of final agreement? Perhaps the clue may be got by twisting a thread from Couty with one from Wolffs. Couty was right when he affirmed the stasis of the blood current, not primarily by overdistention and paralysis of the right heart, but by ineffectual contraction upon an elastic medium and venous reflux through tricuspid insufficiency.

While he admitted in obstruction of pulmonary vessels a possible contributing influence making for stasis, he did not assign to this a sufficiently important role because experiment and deduction combined to mislead him into the belief that, since he found little air *post-mortem* in pulmonary arteries after venous injection, therefore little had entered those vessels. Wolffs having shown that air forced into the pulmonary capillaries does not, as Senn thought, enter the general circulation, but escapes into the alveoli, seems to have supplied, if I may stretch the metaphor, the missing link which connects the threads. The clue is stronger by the two threads than by either alone, and guides to a conclusion. Cerebral and bulbar anæmia is the sole physiological cause of the issue in fatal cases of entrance of air into the veins. The mechanical origin of this anæmia is combined lung and heart stasis in proportions varying with the quantity of air introduced and the time occupied in its introduction. The statement must be thus qualified in consequence of the fact, noted by Cohnheim and interpreted by Wolffs, that, to produce lung independently of heart death, more than half the pulmonary capillaries must be obstructed with air emboli, and that this obstruction must be brusque and not gradual. On the other hand, heart death, unaided, would not occur, because the heart must succumb sooner and by a lower degree of distention

in consequence of simultaneous hindrance to blood propulsion from pulmonary air emboli

There can remain to be noted only those rare exceptions to the foregoing statement, fatalities which are neither cases of lung nor heart death, and which can be explained only by the exceptional passage of air into the greater circulation by way of the pulmonary veins.

In my earlier paper I wrote: "The proximate cause of death has been a subject of much controversy, and it has not yet been explained beyond a doubt;" and after giving a summary of the various views of the authorities then known, I added: "The weight of evidence indicates that one of the chief troubles is the impediment offered to the passage of blood through the lungs." It does not seem that forty years have furnished occasion for much change of emphasis here.

The question already alluded to, of the quantity of air necessary to produce death when admitted into the veins of a human being, is an undetermined one, but must not be disregarded.

I know of no recorded case in which the air found *post-mortem* was measured except that which I have reported above, of Hervieux. In his case the air, collected chiefly from the distended right cavities of the heart, but some of it from the left, equalled in volume from 40 to 45 grams of water. This is definite. A woman died, not instantly but somewhat slowly *post-partum*, and a gas chemically resembling atmospheric air, of a volume equalling 35 to 40 c.c., distending the right heart, was the only cause of death discoverable at autopsy. It does not concern us here whether the gas entered the veins spontaneously or was forced in; whether it was a result of sepsis, or was merely liberated from solution in the blood. We need not too carefully inquire why the state of the pulmonary arteries was not reported upon, nor how a small amount of the gas found its way to the left heart. What we are not permitted to doubt is that the heart was stopped in diastole, and that the distended cavities contained 35 to 40 c.c. of gas twenty-two hours after death. If the pulmonary arteries were likewise distended and their capillaries filled with air or gas emboli, while the ascending cava was charged with frothy blood, such facts would increase the estimated total of gas contained in the circulatory organs at death perhaps threefold or fourfold, and would show that the admission of air or evolution of gas was gradual rather than sudden, and that other mechanical and vital factors, besides cardiac paralysis, might have contributed to determine the character of the symptoms and to promote the fatal issue.

Laborde and Muron found that air injected quickly into the veins of animals caused sudden stoppage of the heart, death by cardiac paralysis. Slow injections by small and repeated amounts the animal supported admirably. Neither slow nor quick, but

gradual, brought lung and brain symptoms before the heart stopped beating.

I give below in parallel columns for comparison the conclusions of a few of the later experimenters, American and foreign, respecting the quantity of air which they found capable of killing dogs. These results vary, but as a whole do not differ materially from those of the investigators who were quoted in my thesis:

ORÉ.	MURON and LABORDE.
60 or 80 or 100 c.c., fatal result.	100 to 200 c.c., *brusque*, instant death.
COUTY.	GOODRIDGE.
80 c.c., *brusque* death; 60 c.c. in weakened dog, death.	75 c.c. for a dog of forty pounds' weight, usually a fatal amount.
SENN.	KOWALEWSKY and WYSSOLSKY.
Dogs weighing about thirty pounds would usually recover after an injection of 30 c.c.; double that amount was generally a fatal dose.	14 c.c. or less at once had killed; 200 c.c. or more in small quantities at a time, borne without disadvantage.
JÜRGENSEN.	WOLFFS.
Slow injection of small and repeated quantities during sixty-five minutes upon a dog weighing 16 kilos, death after 500 c.c.	20 c.c. followed in fifteen minutes by 80 c.c., fatal; 20, 25, and 30 c.c. at intervals covering forty-five minutes, death after 200 c.c. had entered.

I am ready to admit that the fears I formerly expressed regarding the possible mechanical harm from a leaky hypodermic syringe, or from the ordinary operation of tracheotomy, were exaggerated. I do not believe that a bubble of air introduced into a vein is likely to cause alarming symptoms. What may be the minimum quantity capable of doing this in an enfeebled, perhaps exsanguinated, possibly frightened or agitated subject cannot now be affirmed.

Conjectures derived from algebraic formulæ founded on weight and volume comparison in experiments on animals must be delusive.

A statement of Couty is illuminating. After remarking the evidence of cerebral anæmia in animals as only manifest in hurried respiration in the series of observations (the second of his four) illustrating the slightest manifestation of general, and not merely local, trouble, he says: "With man, whose brain is more sensitive, this circulatory trouble, this momentary fall of tension, suffices to produce *a syncope, a momentary loss of consciousness.*" (Italics are Couty's.)

And again he says, after noting the comparative tolerance of some animals: "These accidents are much more rapid with man in whom the heart, we have seen, is more dilatable, in whom the organs are much more dependent, and the brain more susceptible. But even in this more complex organism after the entrance of air the arrest of the central co-ordinators, heart and brain, is not instantaneous; convulsions when they have occurred have super-

vened an appreciable time after the hissing sound—that is to say, twenty or thirty seconds."

The physician cannot overlook the lesson of the larger therapeusis which is constantly enforcing attention to the practical truth that the delicate, nervous equilibrium and the sensitive brain, which accompany the more complex development of the human being, constantly have to be heeded in practice, and must necessarily detach man from comparison with animals, even the superior ones, when there is question of anything in the nature of depressing influence or shock.

It remains but to consider briefly the therapeutics of the subject.

Couty advocated two measures, the one mechanical—bleeding; the other chemical—inhalation of oxygen.

Senn urges, besides indirect treatment by venesection and cardiac stimulants, direct treatment by (*a*) puncture and aspiration of the right ventricle; (*b*) catheterization and aspiration of the right auricle.

These measures he believes to be justified by experimentation as a last resort in all cases where the indirect treatment has proved inadequate to meet the urgent indications. Lauffs, two years later, also suggests puncture of the right ventricle.

Goodridge's experiments were undertaken to determine the therapeutic value of aspiration of the right ventricle, according to the proposal of Senn, combined with venous transfusion of normal salt solution. He concluded that good results may be expected from the combined method of treatment.

The radical direct measures proposed, however well founded in theory and well supported by experiment, are as yet untried in any case of the accident in man.

On the obstetrical side suggestions for treatment are meagre. Some of the more recent books on obstetrics ignore the whole subject; others touch it doubtingly. One of the latest gives reasonable space, but has no word on treatment.

The following remarks are found in the *American Text-book of Obstetrics*: "Very little can be done for the patient even when assistance is close at hand. The cervix should be cleared of clots. Artificial respiration and hypodermic administration of stimulants should be promptly employed. Tracheotomy and the inhalation of oxygen gas, in order to inflate the lungs and to expel the air emboli, have been suggested."

If this utterance be accepted as the concise expression of present-day expert opinion in obstetrics, it follows that the emphasis must be upon preventive measures. These consist wholly in carefully guarding against the risks which recorded experience and tested theory have signalized. It means watchfulness to avoid any conditions which may produce, ever so transiently, a negative atmospheric pressure within the abdomen at the time of expulsion of the contents of the uterus, and for a brief but undetermined period

following. Especially is there need of this if the delivery be rapid, if it be attended or preceded by considerable hemorrhage, if there be placenta prævia, or any need of operative procedures. Care should be taken to follow down the contracting *fundus uteri* with the hand, and maintain manual pressure until continuous tonic contraction is established; to be prudent and conservative in dealing with the third stage, whether delayed or not; to guard the patient against dangerous positions at the time of delivery, and against dangerous change of position or agitation afterward; in a word, and adopting the phrase of M. Hervieux, to "conform rigorously to all the precepts of the art."

I draw the following conclusions: The question being on the occurrence of fatal accidents from spontaneous entrance of air into the veins, those who take the affirmative can accept the burden of proof and urge the paramount importance, in every disputed case, of the *earliest possible* measurements and analysis of the gaseous contents of the veins and heart. This is what the opponents of the proposition have failed to do or even to suggest. Experimental work should also be directed to declare the mechanism of air access to the heart by the channels of the remoter vessels, whether they be the sinuses of the dura mater or the sinuses of the parturient uterus.

These are the problems which claim elucidation, to the end that the theory of accidental fatal air embolism be no longer dependent on testimony however strong, nor on analogy however convincing, but be established on an indisputable basis of demonstration.

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REVIEWS.

A System of Practical Surgery. By Prof. E. von Bergmann, M.D., of Berlin; Prof. P. von Bruns, M.D., of Tübingen, and Prof. J. von Mikulicz, M.D., of Breslau. Edited by William T. Bull, M.D., Professor of Surgery, College of Physicians and Surgeons, Columbia University, New York. Philadelphia and New York: Lea Brothers & Co.

The authors of this "System" have divided their subjects on a topographical basis, so that the surgery of the Head, the Neck, the Thorax and Spinal Column, the Extremities, the Alimentary Tract, and the Pelvis and Genito-urinary Organs is considered in five separate volumes under the above titles.

The book, in spite of the excellent work of Dr. W. T. Bull, the editor, and of the American translators, is in essence an exposition of Continental surgery, and would have no injustice done it if it were labelled "made in Germany."

Just such an exposition in English of German theory and practice is, however, at this time of distinct value to American practitioners and to teachers too busy to consult the original writings of the distinguished authors, although it should be regarded as supplementary to the standard English and American "systems" and text-books.

If any one body of surgical authors or practitioners were to be selected to-day as the chief authority, the court of last resort, in surgery it would not in the opinion of the writer be found anywhere east of Greenwich or west of San Francisco. It was, therefore, somewhat of a disappointment on reading this book to note the almost exclusive reference to German views, methods, statistics, and experiences. Of those views, methods, etc., it is, however, a most interesting, complete, and useful exponent, and, after all, there probably was never a time during the period covered by modern surgery—*i. e.*, the period since Lister introduced antisepsis—when there were so few radical differences as there are now among surgeons of differing nationalities.

In Volume I. the most important article is that on Injuries and Diseases of the Skull and its Contents, by von Bergmann and Krönlein. It is most instructive, and while it may now seem to err in the direction of conservatism, it is not improbable that its

somewhat dogmatic teachings may later become the accepted views of the profession.

The statement that in fractures of the base, the prognosis is more unfavorable than in fractures of the vault "because the accompanying brain lesion is deeper and more extensive," should be extended to include the greater risk of infection due to the impossibility of ensuring sterility of the nose, pharynx, and auditory canal.

The usual advice to trephine in cases of "funnel-shaped fractures," even although in so doing a simple fracture is converted into a compound one, is qualified by the statement that "whenever" such a fracture or a narrowly limited depressed fracture is combined with localized brain symptoms, the depressed, splintered, cone-shaped fragment of bone must be removed, whether in case of a simple or compound fracture; and further, by the remark that neither the authors nor other observers have ever seen a funnel-shaped depressed fracture occur without a wound of the soft parts.

The existence of localized brain symptoms, or of irritation in these cases, is emphasized because the authors believe that narrowly limited depressions never cause symptoms of compression of the brain, no matter how deep they may be, for "the diminution of intracranial space brought about by the projecting cone-shaped fragment of bone is never sufficient to disturb the circulation of the brain and its membranes." They add that "depressions limited to a small area have been held responsible for subsequent *epilepsy*, and to remove or elevate depressed areas of bone in every case has been considered positively indicated. As a matter of fact, epilepsy occurs as frequently in connection with head injuries in which no fracture exists. Depression is no more a factor in the etiology of this disease than any other scar of the brain or external soft parts that has become adherent to the skull."

Gunshot wounds of the skull are considered with sufficient thoroughness, but it is to be noted that the article dealing with them is based upon the work of Kocher and von Bruns, and upon that of von Coler and of Schjerning in the "Imperial Royal Prussian War Department." No reference is made to the British or American experiences in the South African and Spanish wars.

"Undubitable," page 87, and "acustic," page 92, may be intentional, but are probably typographic slips.

In Volume II. one of the most interesting of the articles is that upon Goitre, by von Eiselsberg. The author believes that medicinal treatment in goitrous cases should at present consist exclusively in the use of iodine, and adds: "The action of this drug is certain. According to Kocher, 90 per cent. of all goitres may be improved by the use of iodine to such an extent that operation will be unnecessary. The efforts of pharmacology are not directed to finding a substitute for iodine, but to the use of the best preparation." He

includes the treatment of goitre with thyroid substance, or with preparations of it, as a modification of the iodine treatment, because Baumann's experiments have shown that iodine is contained in the active principle of the thyroid gland. He cites the experience of von Bruns, who administered 5 to 15 grains of the gland daily in the form of tablets to 350 patients, and reported 8 per cent. of complete cures, 36 per cent. of good effects, 30 per cent. of moderate success, and no success in the remaining cases. When he adds, however, that a number of authors report cases in which this treatment was productive of no result whatever, he might safely have included the large majority of American surgeons in whose hands the thyroid treatment and the iodine treatment have been exceedingly unsatisfactory.

A no less interesting article on the Thorax and its contents, by von Riedinger and Kümmell, deserves mention for its thoroughness and clearness.

In the section on Carcinoma of the Mamma, the noticeable increase of cancer in all countries is commented on; and in Prussia the death rate from this disease is said to have increased 153 per cent. since 1877. The authors do not believe that local recurrences after operation are due to infection with cancer cells at the time of operation, although they do not deny that this may be possible. In considering the improved results of recent years—unquestionably due to earlier as well as to more extensive operation—not enough emphasis is placed on the former factor, which is the more important of the two.

It is interesting to note the statistics of so-called permanent cures —*i. e.*, cures in which three years have elapsed without recurrence. These vary from 19.4 per cent. (Horner) to 42 per cent. (Rotter, Heidenhain). In the writer's opinion the three-year period, while convenient as an arbitrary basis for description of results, is illusory if considered as justifying the literal use of the term "permanent cure." The teaching that cancer of the breast in its early stages is a local disease, that a permanent cure is possible by radical removal of the tumor, and by that method only, that the condition never gets well of itself, and that the value of other methods of treatment is extremely doubtful, would be subscribed to by the vast majority of surgeons everywhere. Thorough and radical operation is recommended, but the methods in which all the infra- and supraclavicular glands are removed, suggest to the authors the remark that it is doubtful whether the success in operations of this sort is proportionate to the severity of the interference, because in these cases the intrathoracic lymphatics are almost certain to be diseased. Heidenhain's and Stiles' investigations have shown how very much more extensive lymphatic infection may be than the evident metastases would seem to indicate. "In carcinoma with involvement of the clavicular gland therefore the operation in

all probability will be done too late, and a permanent cure extremely doubtful."

On page 301, parenchymatous "stroma" should be "struma."

In Volume III., devoted to the surgery of the extremities, occurs perhaps the most conspicuous example of the inconvenience of the topographical division of the subjects. Fractures, for example, are not found as a separate section, but must be hunted up under the surgery of the various regions. Such inconvenience is necessary in works on applied anatomy, but is objectionable in surgical text-books.

As a rule, surprisingly little difference is to be observed in the apparatus recommended in the treatment of these injuries. It has not been long since a German text-book in treating of fractures of the thigh would have devoted pages to cumbrous and antiquated splints. Here, Hoffa, while mentioning the exceptional cases in which special apparatus is required, says "the various immobilization splints and apparatus formerly used often did more harm than good, and are replaced at the present time by position-, strip-, and plaster-splints and continuous weight extension." If, however, any mention is made in the consideration of ununited fracture of this and other bones of the most valuable mechanical addition to our methods of treatment—Parkhill's splints—it has escaped the notice of the writer. For example, in discussing pseudarthrosis after fracture of the shaft of the ulna, Wilms says that of the various methods proposed to stimulate ossification, he "will mention only the insertion of ivory pegs and suture of the bone," both of which have been found by surgeons in this country to be relatively very unsatisfactory except in cases of extremely oblique fracture where the two fragments may readily be transfixed. Even then a simple screw or gimlet is superior to either of them.

In the article on Amputations no description is given of what many surgeons regard as the best method of performing what is probably the most frequent of all amputations—the amputation of the leg—the method which secures a periosteal flap without disturbing the relations of the deeper structures. The methods of Bier and Storp involve the retention of a "bone hinge plate," which is an unnecessary and clumsy complication of the operation. Unqualified approval may be given to the statement that if the surgeon is uncertain as to whether the tissues are infected or not, or if speed is required in severe accident cases, "it is urgently recommended not to close the wound, but to pack with sterile or iodoform gauze after checking the bleeding, to apply a dressing with slight pressure, and to close the wound secondarily."

In discussing the prognosis of amputation of the arm, the same writer says that the mortality in uncomplicated cases is "practically *nil.*" This favorite but slovenly expression is objectionable. In this, as in other surgical procedures, either there *is* a mortality, in

which case it is not "*nil*" whether viewed from a "practical" or from a theoretical standpoint; or there is *no* mortality, which fact is susceptible of clear statement in English.

On page 163, the legend under Figure 103 describes it as an "*X*-ray of Figure 103." It should probably be of "Figure 102." On page 541, "counterindicated" should, we think, be "contra-indicated," although the former word is used throughout by the majority of the translators.

Volume IV. contains an exhaustive series of articles on the Surgery of the Alimentary Tract. In the article on the treatment of hernia (Graser), Czerny's operation is first mentioned and is said to be the simplest. Bassini's operation is imperfectly described, and is illustrated by somewhat clumsy wood-cuts, and rendered more confusing by the description which in Figure 229 begins "Operation for the cure of oblique inguinal hernia," and in Figure 230, shows the "strangulated contents" of the sac.

Halsted is not mentioned. Various operations now regarded by most surgeons as obsolete, such as Macewen's, are described with no expression of opinion.

The statistics of operations for radical cure would seem to show only about 10 per cent. of recurrences. It is very doubtful whether this is correct, the recorded results varying greatly with the age of the patients, their general health, their subsequent occupation, and the time at which the report is made.

Schlange's operation on Appendicitis is of special interest. Two of a series of rules which he gives may here be quoted: "There is a relatively large group of cases of appendicitis in which the attack is from the start of slight character. Since the general condition of the patient is little affected, there is not much infiltration of the tissues and the fever is slight or becomes so by the third day. In such a case an operation is counterindicated, although the patient or his nurse should be advised that it may become necessary at any time. Furthermore, one should point out the probability of recurrence so that operation in the interval may be performed if desired."

"Whatever the skill of the operator, he should not insist upon removal of the appendix if it is so situated that its removal will greatly complicate the operation."

These are singled out because of their relation to questions still under dispute. Unequivocal disapproval should be given to the teaching to give the patient in the early stages, "before the diagnosis is certain," "a moderate amount of opium, and if necessary, morphine to control the pain." He adds: "Cathartics and large rectal injections are inadvisable since they stimulate peristaltic action and may drive fluid fecal matter through the perforated appendix." This has been abundantly shown to be a purely imaginary danger. The reviewer has never seen a case of death from appendicitis

which could be remotely attributed to the administration of laxatives in the early stages. He has seen many such cases in which the fatal result was due to the use of opium.

Volume V. deals with the Genito-urinary Tract and the Pelvic Organs. As a rule, the teaching is sound, but in some places seems to be antiquated. The statement that "suprapubic cystotomy should be chosen for the removal of vesical calculus in a boy under fourteen years of age" cannot be allowed to pass without question. It certainly does not represent the views of English or American surgeons at this time.

Freyer's operation for the total removal of the prostate is not mentioned, and the author says: "A study of the anatomy of prostatic hypertrophy makes it somewhat doubtful whether one ought ever to attempt to remove an enlarged middle lobe of the prostate through the bladder!"

As to the "sexual operations" for enlargement of the prostate, he says truly that "it is fair to conclude that sexual operations," meaning thereby both castration and substitutes for it, "have not fulfilled the hopes of their originators;" and adds that "in view of the surrounding circumstances, and of the imperfect results thus far obtained, it may be stated that sexual operations yield no better results than other operative measures, and that, therefore, they should only be performed under special conditions."

Why he should have classed ligation of the internal iliac arteries with the sexual group of operations it is difficult to say.

The article by Schede on the examination of the kidney and ureter is a very practical and instructive one, and has been brought well up to date.

Steinthal's article on the Surgery of the Rectum is another one well deserving of favorable mention. In carcinoma, he regards early operation as determining the degree of success which may be obtained. In prolapsus, he recommends cauterization of the superfluous membrane. In the treatment of hemorrhoids he compares excision and cauterization, and describes the use of the ligature in only a few lines, adding that "it is claimed that suppurating thrombophlebitis and pyæmia may follow this operation." This is a very unfair presentation of the case. His own figures show that while Allingham has treated 1600 patients by this method without a fatality, Mikulicz has lost after excision two cases out of one hundred and thirty.

The general appearance of the book is most pleasing; the illustrations are numerous and usually adequate to the elucidation of the text; the rendering into English has been admirably done and reflects credit on the scholarship of the translators; Dr. Bull's name is sufficient evidence of the excellence of the editing.

If the publishers instead of saying "the special features wherein American surgery differs from that practised in Europe are fully

reflected," had said that the points wherein German surgery differs from that practised in America were fully set forth; and if instead of saying that "these five volumes constitute a complete working library on Surgery," they had said that no working library on Surgery could be considered as complete without them, the reviewer would cheerfully have subscribed to their not otherwise extravagant commendation of this most excellent "System." J. W. W.

EPILEPSY AND ITS TREATMENT. By WILLIAM P. SPRATLING, M.D., Medical Superintendent of the Craig Colony for Epileptics; Secretary of the National Association for the Study of Epilepsy and the Care and Treatment of Epileptics; Member of American Medico-Psychological Association, New York Academy of Medicine, Buffalo Academy of Medicine, Rochester Pathological Society, American Medical Association, etc. Fully illustrated. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

THIS volume of 500 pages treats the subject of epilepsy thoroughly from every point of view. Coming from the pen of one with Dr. Spratling's experience with this disease it is sure to fill an important place in the literature upon epilepsy. The method employed by the author is to give a review of the literature followed by an account of his own experience in each topic discussed, showing where his own researches substantiate or disagree with the ideas generally held. Many cases are used for means of illustration.

The subject is treated under the usual heads of Definition, Classification, Etiology, Diagnosis, Prognosis, Pathology, Treatment and Psychological and Medicolegal Aspects, and the arrangement of the book is excellent. It should prove very satisfactory as a book of reference, tables and classifications being numerous.

The chapter on Status Epilepticus has been written by L. Pierce Clark, M.D., who has, together with Thomas P. Prout, M.D., written the chapter on the pathology of epilepsy. Both of these chapters have separate bibliographies. In the latter the authors largely base their opinions on investigations carried on at the Craig Colony for Epileptics, and consider that the disease may be regarded as a highly organized sensory motor reflex of the cerebral cortex. The chapter on prognosis is of interest in that it takes up the importance of various conditions which mark cases as curable or incurable. Spratling's statistics show that at the Craig Colony 5 per cent. of the 643 possible curable cases have recovered.

The author divides treatment into general, medical, and surgical, and under the first division lays special emphasis on the Colony

method of treatment, where not only the disease but the individual is recognized and treated, a factor which he considers very important.

The book is if anything too comprehensive, and includes some matter that could be omitted. Such is especially noted in the chapter on Surgical Treatment, where detailed descriptions of the technique of trephining and abdominal section are gone into. The literary style is straightforward and clear. As it is the first American book to appear upon the subject of epilepsy for thirty-three years its appearance should be welcomed. Treating as it does such an important disease in a very lucid and thorough manner it is sure to be of much value. C. C. R.

A Treatise on Materia Medica and Therapeutics, including Pharmacy, Dispensing, Pharmacology, and Administration of Drugs. By Dr. R. Ghosh. Edited by Lt.-Col. C. P. Lukis, M.B. Calcutta: Hilton & Co.

Although this work is primarily intended for East Indian students and physicians, it is nevertheless one which possesses its value for readers in other countries. The material contained in it is so arranged as to make it of the greatest practical value as a ready reference handbook. There are several novel features which appeal strongly to the practising physician, among which we would particularly mention what the author terms "prescribing hints," which tell us in what manner the various remedies may be most elegantly prescribed. These hints are appended to the description of the more important drugs. The work follows the British Pharmacopœia, but has in addition a very complete account of the medicinal preparations which are contained in the Indian edition to that work. Many American authorities would do well to adopt the excellent classification and practical arrangement which is found throughout this book. J. N. H.

Normal Histology. By Edward K. Dunham, Ph.B., M.D., Professor of General Pathology, Bacteriology, and Hygiene in the University and Bellevue Hospital Medical College, New York. Third edition, revised and enlarged. Illustrated with 260 engravings. New York and Philadelphia: Lea Brothers & Co., 1904.

The present edition of this book is to be highly recommended. Short, concise and clearly written it forms an excellent supplement to the student's practical work in this branch of his medical educa-

tion. Since the volume is not intended as a book of reference the reader is referred to larger treatises, and anatomical journals for a more extensive survey of certain subjects which cannot here be treated in a broad manner. The main facts and important principles concerning the cells, the tissues, and the various organs are very clearly stated. The ductless glands, so grossly ignored in the older text-books, receive appropriate space. The histology of the nervous system is dealt with in an elementary manner but this cannot be considered as a fault, since the subject is too large to admit of extended treatment except in a volume devoted especially to this phase of anatomy. The organs of special sense, too, are described in 12 pages. The final chapter on Histological Technique scarcely seems necessary for books devoted exclusively to this subject are readily obtainable for class-room work and give a much more extensive view of technical methods than can be put into the short space used by the author. Most of the illustrations are good, and the cuts adapted from other text-books have been, as a rule, well chosen. W. T. L.

NERVOUS AND MENTAL DISEASES; A MANUAL FOR STUDENTS AND PRACTITIONERS, WITH AN APPENDIX ON INSOMNIA. By JOSEPH DARWIN NAGEL, M.D. Philadelphia and New York: Lea Brothers & Co., 1904.

THIS is a good little book for a student to use to prepare for a quiz or to work up for a theoretical examination. It is of the class that a conscientious teacher regards with more or less justifiable suspicion and that the student utilizes as a very present help in trouble. It is much better than the quiz compends, because it gives coherent and, so far as is possible in such limited space, accurate descriptions of diseases. There is, unfortunately, owing to our methods of teaching, a period in the life of every medical student when he must learn certain things by mere force of memory and without the use of reason. For that period this book is a very good one. For the practitioner it will be found a convenient compendium for ready reference. C. W. B.

CLINICAL LECTURES ON MENTAL DISEASES. By T. S. CLOUSTON, M.D. Edin., F.R.C.P.E. Sixth edition. Philadelphia and New York: Lea Brothers & Co., 1904.

A BOOK that has passed through six editions, and has been before the public as long as this, little needs reviewing. It has proved its worth. We must say, however, that it is a great pleasure in these

days, when so many books are merely manufactured like shoes or sausages, to read one that has really been written, and that by a man who speaks from his own knowledge and pays attention to the rules of grammar. Clouston is somewhat old-fashioned. For example, the word paresis does not occur in the index, the term general paralysis alone being used. Paranoia, which in most books of to-day occupies many pages, here has little more than two, but much concerning it is discussed under monomania. Maniac depressive insanity is not mentioned in the index, and nothing is said about the association of insanity with certain types of neuritis. We mention these omissions not in disparagement of the book, but to show its scope and the point of view of the author. The book is most interesting and valuable and gives excellent pictures of insanity. This edition differs from the earlier ones very markedly in the sections on pathology. C. W. B.

THE DOCTOR'S LEISURE HOUR. FACTS AND FANCIES OF INTEREST TO THE DOCTOR AND HIS PATIENT. By CHARLES WELLS MOULTON, General Editor. Arranged by PORTER DAVIES, M.D. Chicago, Ohio, and New York: The Saalfield Publishing Co., 1904.

THIS book, compiled by a doctor in his leisure hours for the amusement of other physicians in theirs, contains a curious hodgepodge of jokes, stories, and poems gathered from newspapers and other periodical literature, intermingled with a few borrowed from the literature of a higher class; thus we find extracts from the works of Molière and Oliver Wendell Holmes mingled with jokes and poems such as pass current for wit in the pages of our daily newspapers. Many of the anecdotes have figured in other collections of professional ana such as "The Gold-Headed Cane," and Jeffries' famous "Book about Doctors." Although there are many extracts in the collection which reflect credit upon the profession, nevertheless we doubt if it is wise from a physician's point of view that such a collection should ever fall into the hands of the laity. It is bad enough to be compelled to read the cheap witticisms on appendicitis, faith cure, and Christian Science which are now so current in the daily press, without having them gathered in a quasi-respectable form. It is good that such collections of medical ana should be published occasionally, as there is much gold among the baser metal which they contain, and we think this book will probably achieve, as it deserves, a very considerable popularity in the ranks of the profession. F. R. P.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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Gonorrhœal Phlebitis.—JULIUS HELLER (*Berliner klin. Wochenschrift*, 1904, xli., 609) reports a case of gonorrhœal phlebitis of the posterior saphenous vein and of the pampiniform plexus of veins on the left side coming on four weeks after all urethral symptoms of a rather severe attack of gonorrhœa had subsided. He further reviews 25 cases he has been able to collect from the literature; 20 of the cases were in men, 6 in women, and all but 2 occurred in the decade from twenty to thirty years of age. In all but 1 case the complication accompanied the first attack of gonorrhœa. The phlebitis usually occurs in the subacute stage of the urethritis, the average period of incidence in fifteen observations being four and one-half weeks after onset. In 1 case it came on fourteen days after onset, and in 3 others three, sixteen, and eighteen months after, respectively. The original attack of gonorrhœa may run an uncomplicated course, but it is more often severe and associated with complications—prostatitis, urethrocystitis, epididymitis, pleuritis, pyelitis, and erythema nodosum being reported; 15 of the cases were accompanied with arthritis.

The veins affected were as follows: the common iliac (side not mentioned), 1; the internal iliac (side not mentioned), 1; the femoral: right, 3; left, 3; the popliteal (side not mentioned), 1; the deep femoral: left, 2; side not mentioned, 1; the internal saphenous: right, 9; left, 6; side not mentioned, 1; superficial abdominal veins (side not mentioned), 3; vaginal veins: left, 1; dorsal vein of penis, 1; vein to the corpus cavernosum, 3; prostate and vesical veins, 2; pampiniform plexus: right, 1; humeral vein: right, 3; left, 1; radial and cubital veins: left, 1. In most cases a single venous system is affected; in only 6 cases separate systems. Fever was present in 10 cases, in 1 continuous and resembling somewhat a typhoid curve. In 2 cases chills were noted. The outcome of the phlebitis is usually a complete *restitutio ad integrum;* this was the case in 16 cases—62 per cent. The duration in these cases

varied from a few days to ten weeks, with an average of six weeks in ten observations. Occasionally, however, the cure is not so complete. In Empe's case the vein was still obliterated and œdema present after three months, and in the cases of Monteux and Lops there was persistent induration of the affected vein. In Hasemud's case amputation of the thigh was necessary. Pollard's patient died of pulmonary embolism.

Heller ascribes phlebitis in these cases to the gonococcus, although the fact has not been established anatomically. He suggests that in the cases with high fever and marked constitutional symptoms there may be a mixed infection.

Dysbasia Angiosclerotica (Intermittent Claudication).—W. Erb (*Münchener med. Woch.*, 1904, li., 905) reports 45 cases of this interesting condition as a supplement to his original publication in the *Deut. Zeitschr. f. Nervenheilk.*, 1898, xiii., 1–76.

In 38 cases the condition was typical—intermittent exhaustion on walking, with rapid resuscitation after rest; in 7 cases atypical, the intermittent claudication being replaced by symptoms only suggestive, as weakness and rapidly manifested fatigue, pain in the legs on exercise, with paræsthesias and sensations of cold. In all of these cases, however, there was the characteristic complete or incomplete obliteration of the pulse in the arteries of the feet and well-marked general arteriosclerosis. In 30 cases the condition was bilateral; in 15 unilateral, with marked selection of the left side—11 to 4. Of the 30 bilateral cases all four of the pulses were absent in 16 cases; three in 2 cases; two in 7 cases; one in 1 case. In the remaining 4 cases the pulse was palpable, but very weak. Of the 7 unilateral cases both pulses were absent on the affected side in 5 cases; one absent and the other weak in 1 case, and both palpable in 1 case. In 2 cases both of the pulses were absent even on the apparently healthy side, and in 4 more one pulse was absent on the symptom-free side. In some instances the popliteal pulse was obliterated, and in a few even the femoral.

The associated general arteriosclerosis was variable. In 8 cases it was only slightly marked or even absent, while in the remaining 37 it was very evident in the peripheral arteries, varying from moderate to most extreme grades. None of the cases were associated with granular kidneys—at least in only one was this a possibility—and only 2 showed albumin in the urine. Cardiac changes could be demonstrated in but 15 cases, the changes consisting in an accentuated second aortic, a systolic murmur, slight left ventricle hypertrophy, an irregular or intermittent pulse, and in 1 case attacks of angina pectoris. Vasomotor disturbances—cold feet, pallor, flushing, cyanosis, etc.—were observed in 32 cases, absent in 11. Two cases had gangrene. Neurasthenia was a prominent symptom in 5 cases, but the examination of the nervous system was normal in all 45, excepting 1, in which the Achilles tendon reflex was absent, and a concurrent spinal affection could not be definitely excluded. Erb has met with cases in which, with typical symptoms of intermittent claudication, the arteries were apparently normal and the pulses well felt. These he refers to as purely neurotic (vasomotor?) forms of the affection. On the other hand, patients are encountered with entirely or almost absent pulse in the tibial arteries who are perfectly free from symptoms.

All of Erb's 45 cases were males, and of 81 cases collected from the literature only 6 were females. The age of the patients at the onset of symptoms was: under thirty years, 1 case; from thirty-one to forty years, 7 cases; from forty-one to fifty years, 16 cases; from fifty-one to sixty years, 12 cases; from sixty-one to seventy years, 9 cases. Previous syphilitic infection was present in 10 cases—22.77 per cent. This cannot be considered of etiological moment, as in the statistics of 10,000 men over twenty-five years of age Erb found a history of syphilis in 21.5 per cent. 32 of the cases used alcohol moderately or not at all; 7 cases admitted excesses, and in 6 there is no note of the habit. 15 cases gave a history of excessive smoking, and 10 of heavy smoking; 13 smoked moderately or not at all, and in 7 cases the relation is not noted. Erb is inclined to lay much emphasis on the abuse of tobacco as an etiological factor. 12 cases gave positive history of exposure to cold, 6 of these being inhabitants of Russia; 2 cases had gout, 2 diabetes, and 1 lead-poisoning. As possible influencing factors are further mentioned the abuse of coffee and continuous pressure on the femoral artery by a truss for the control of rupture.

[The reviewer has now under observation a most typical example of intermittent claudication of the left leg following an acute arteritis with probable parietal thrombosis of the femoral vein in typhoid fever. Reference may be found to the case in an article on the "Cardiac and Vascular Complications and Sequels of Typhoid Fever," in *Johns Hopkins Bulletin* for October, 1904.—W. S. T.]

The Occurrence of Herpes Zoster in Croupous Pneumonia.—Dr. Riehl (*Münch. med. Woch.*, 1904, li., 1105) states that in 481 cases of croupous pneumonia herpes was noted in 129 cases, or 26.82 per cent. This is a little below the figures usually quoted, Drasche giving 40 per cent.; Metzger, 43.2 per cent.; Smaler, 32 per cent. Of the 129 cases 99 were males and 30 females. The occurrence of herpes is most common in robust patients in the second and third decades, and notably infrequent in the very young and very old. Following the usual rule the eruption occurred most often on the third, fourth, and fifth day of the disease, followed soon after (two to four days) by the crisis; not infrequently, however, it appeared on the second or was delayed until the ninth or tenth day, and in one instance it appeared on the twenty-sixth. Recurrence of the eruption during convalescence, as was reported by Bleules in 9 cases, was not noted by Riehl. The pneumonia proved fatal in 70 out of 481 patients, and of these 70 only 6 had an eruption of herpes. This distinctly emphasizes the favorable prognostic significance of the eruption, a significance previously insisted upon by many observers. Herpes is usually most abundantly developed in the mildest cases of pneumonia. The figures in reference to the distribution of the herpes are interesting enough to quote in full. In 88.36 per cent. of the cases the eruption occurred in the region of distribution of the second or third branches of the trigeminus. The upper lip was involved in 25 cases; upper and lower lip, 24; upper lip and angle of mouth, 1; upper lip and nose, 7; upper lip, under lip, and nose, 3; upper lip, angle of mouth and nose, 2; upper lip and chin, 1; upper lip, under lip, and chin, 1; lower lip, 16; lower lip and angle of mouth, 4; lower lip and nose, 2; nose and nasal septum, 15; angle of mouth, 8; angle of mouth and chin, 1. The eruption occurred on the same side as the

pneumonia twelve times; on the opposite side twelve times. In 46 cases of right-sided and 39 cases of left-sided pneumonia it was localized on both sides; in 17 cases of double pneumonia it occurred three times on the right side; three times on the left side, and eleven times on both sides. As unusual localizations, herpes may be mentioned on the tip of the tongue, once; on the ear, three times; on the forehead, twice; and on the upper eyelids, twice.

SURGERY.

UNDER THE CHARGE OF

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AND

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The Technique of the Use of Venous Hyperæmia.—HENLE (*Centralblatt für Chir.*, 1904, No. 13) states that in the use of venous hyperæmia one has a valuable antidote against tuberculosis of the extremities, as has been clearly shown by the experiments that have been conducted in the Breslau Surgical Clinic. That it also is effective in either chronic or acute affections of the joints has been proven by many experiments. Its value in erysipelas has been well shown in many cases. Bier found as the result of his experience that the best results are to be obtained by only producing a hyperæmia for the space of one hour daily. Care should be taken that the arterial circulation is not interfered with, and the best results have been obtained not by using the Esmarch bandage, but by the use of a band similar in its construction and application to that which is found as a part of the Riva-Rocci blood-pressure apparatus. By the use of this special apparatus, which the author has designed, the pressure can be most accurately regulated, and the degree of venous hyperæmia easily controlled.

The Diagnosis and Treatment of Hemorrhoids.—BRICK (*American Medicine*, July 23, 1904) after an admirable and most complete review of the surgical treatment of this most common condition states in conclusion that the method selected should be the one best suited to the individual case, although no case of internal piles that has come under the author's observation has been too severe for the clamp and cautery method. There is a double protection against hemorrhage both by the crushing action of the clamp on the tunica intima and by the cauterization, the thermic action of the cautery destroying all septic germs which may be present on the operative field; all capillaries and lymphatics are sealed, which prevents absorption of septic agents; there are no ligatures to cut through; the operation is finished at one time; no

protracted inflammation from injured nerves; no sutures to be removed, and there is a gain of about one week in the time of healing.

The Treatment of Chronic Bright's Disease.—ROVSING (*Centralblatt für Chir.*, 1904, No. 17) states that in a previous publication Edebohls has misquoted some statements and attributed them to him, and with a view to clearing up the facts it becomes necessary to again go into the question in detail.

Edebohls has stated that in his opinion there should be total extirpation of the membrana propria if the kidney and its capsules are either partially or totally diseased, so that there may be union between the surface of the kidney and its surrounding fat capsules.

Rovsing entirely disagrees with this view, for the reason that when this is done the kidney becomes embedded in a mass of newly formed connective tissue which, when new, guarantees an ample supply of blood, but later these adhesions of necessity retract and atrophy, and, as a result, the blood supply to the kidney is distinctly impaired and the kidney consequently undergoes atrophy. In Rovsing's opinion capsulectomy is only indicated in those cases where the kidney is either partially or totally bound down by adhesions, or if the kidney be tense and markedly swollen, or the membrana propria is distended by cysts. Such a condition is more often found in those cases where there is either a nephritis complicated by infection, or in nephrolithiasis, or in those cases which may be described under the name of a curative aseptic interstitial nephritis and perinephritis, and which may be recognized by pain in the region of the kidney, and in which pain rarely may be accompanied by hæmaturia. The pain in these cases is due to an irritation of the membrana propria, which is supplied by large numbers of sensitive nerve filaments. In Rovsing's judgment operation is only indicated in cases of nephritis dolorosa. In those cases where marked toxic conditions exist operation is not only not indicated, but in the majority of instances is extremely dangerous. In opposition to these views, Edebohls has taken the stand that in every case of chronic Bright's disease, no matter in what condition it may be, both kidneys should be subjected to decapsulation. Rovsing insists that in his judgment this is so grave an error as to require emphatic protest from the surgical as well as the medical point of view. It may be laid down as a broad general rule that each case must be considered upon its merits, and no case should be subjected to operative interference until it has been subjected to the most careful examination. Every case is not a suitable case for operation. It is to be regretted that a search through the literature shows that in the reports on the surgical treatment of Bright's disease no mention is made in many cases that there has been the careful and thorough examination, which should be the invariable rule before subjecting a patient to all the risks of operation. No one has been more to blame for this than Edebohls, as may be clearly seen by a reference to his article in the *Medical Record*, December 21, 1901. And a further examination of this article will show that out of eighteen cases not one of them has been subjected to a cystoscopic examination of the bladder with catheterization of the ureters and a subsequent bacteriological examination of the fluid obtained. The history of these cases is also lacking in many things, such as the exact amount of albumin the urine contained, and also the results of a careful micro-

scopic examination of the urine after sedimentation. The diagnosis in many of these cases would seem to have been obscure, and it appears to have been based upon two points: First, albuminous urine; and, second, inspection of the kidney through the small lumbar incision of Simon; but when one considers how often the floating kidney is complicated by albuminous urine from purely mechanical or infectious conditions, besides in many cases being found to be either atrophied or swollen, or the membrana propria adherent by reason of traumatism, it makes one extremely doubtful in the view of these facts as to whether or not a correct diagnosis had been arrived at in all of the cases which Edebohls subjected to operation; and this skepticism becomes of necessity more marked when one becomes aware of the fact that Edebohls reports that in nine out of these sixteen cases the other kidney was absolutely healthy, the Bright's disease being merely confined to the one side; and the subsequent note that immediately the kidney was sutured the albumin disappeared. Of the eight patients whom Edebohls reports as cured, in seven of the cases only one kidney was affected.

There is only one conclusion that can be reached in view of these facts, and that is the albuminuria has been due simply to the undue mobility of the kidney, and this has been relieved by suturing the kidney in its proper position in the loin. In only two of the cases was decapsulation performed. Neither of these patients had Bright's disease, and the result was that one of them died and the other is reported as not cured. It is of interest to see Edebohls' further reports upon this subject. In the *Medical Record* for March 28, 1903, he notes that at the end of the year 1902 he had operated upon not less than fifty-two cases of chronic Bright's disease, and that of these cases eleven died and not a single one was cured. It would, therefore, seem perfectly proper after due consideration to intimate that Edebohls has not given to the profession a single shadow of proof that chronic Bright's disease can be cured by operative interference.

Out of ten cases of chronic Bright's disease which Rovsing treated by decapsulation, there is not a single case in which a cure has been the result, and common-sense would seem to show that when one considers the pathology of the disease operative interference will be of no avail. Too much stress cannot be laid upon the fact that in Rovsing's judgment operative interference is absolutely contraindicated, except in those rare cases of chronic Bright's disease which are accompanied by severe kidney pain; and also in those cases of nephritis which are either traumatic, infectious, or dependent upon the irritation of uric acid for their origin. Therefore, it is absolutely essential that every case should be subjected to a most prolonged examination in order that the etiology of the nephritis may be clearly determined before any operation is decided upon. Too much stress cannot be laid upon the great importance of this careful early examination, which should include microscopic and bacteriological examination of the urine obtained by catheterization of the ureters.

The Treatment of Fractures of the Lower End of the Femur by the Bardenheur Method.—Graessner (*Centralblatt für Chir.*, 1904, No. 11) states that the splendid results of this method in the treatment of supracondyloid fractures of the humerus has induced him to try this method in those fractures of the femur in which there is marked

deformity. Experience, which has been confirmed by *x*-ray pictures, shows that the deformity can be completely overcome by a weight of 25 kilograms in men and 20 kilograms in women. The subsequent examination of the patients who have been subjected to this method of treatment has shown that good union is secured without the shortening which seems inevitable under other methods of treatment.

THERAPEUTICS.

UNDER THE CHARGE OF

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Hyperchlorhydria and its Treatment.—Dr. B. H. Trago believes that hyperchlorhydria is a disease, not a symptom. In treatment we should first prescribe a milk diet. Antiseptic medication causes a cure in certain cases. The physician should remember how the disease develops and the therapeutic indications which may arise. Gastro-intestinal anastomosis is a last resort. This operation is not applicable in the treatment of all cases of hyperchlorhydria with pyloric spasm. Lastly, the mixed medical treatment is the one which will result in the largest number of cures.—*Revue de thérapeutique*, 1904, No. 15, p. 525.

Dechloration in Hysteria.—M. Vincent is of the opinion that sodium chloride in excess not only affects the stomach and kidneys, but aggravates the tendency to hysteria in patients who tend to high nervous excitability. If hysterical persons are given three to four drachms of salt per day, in addition to their regular allowance, the nervousness is increased and the number of hysterical seizures augmented. Likewise, salt appears to excite persons affected with latent hysteria. At the same time gastric disturbances, insomnia, and other signs of hysteria become more apparent. On the other hand, upon a diet lacking in salt these symptoms tend to disappear. Thus, salt in excess plays the same part in hysteria as alcohol, lead, mercury, etc., and exaggerates any hysterical tendency. In patients who are affected with hyperchlorhydria as well, diminishing the chlorides will act favorably upon the stomach as well as upon the system in general.—*La semaine médicale*, 1904, No. 28, p. 221.

The Choice of an Acid for Gastric Medication.—Dr. Alfred Martinet, after a discussion of the various acids that may be employed, concludes that hydrochloric and phosphoric are the only ones admissible; he is strongly in favor of the latter, since it possesses the following advantages: It does not lessen the secretion of hydrochloric acid in the stomach. It is quickly neutralized in the intestine and changed into sodium phosphate, a normal constituent of the blood. It is elim-

inated, at least in part, by the kidneys as acid sodium phosphate, a normal constituent of the urine. It lessens the acidity of the urine and contributes toward rendering the urinary tract aseptic. It acts on the nervous system as a tonic, especially in dyspeptics, and the results achieved by its use justify its employment. The author gives the following formula: official phosphoric acid, 10 parts; acid sodium phosphate, 20 parts; water, 200 parts. Dose, one-half to two teaspoonsful in a glass of water, wine, or beer, to be drunk during the mid-day and evening meals. Its administration may be continued for long periods without the least bad effect.—*La presse médicale*, 1904, No. 59, p. 469.

Gastric Lavage in Infants.—Dr. J. Cassel states that gastric lavage has limited indications in pediatric practice. It is, however, especially useful in gastric atony caused by inappropriate feeding, particularly when the food is too watery or too abundant. The child should be fed at intervals of about four hours, and three hours after a feeding, the quality and quantity of which have been carefully noted, what remains in the stomach is drawn off. The procedure is kept up until the food has been so altered that none is left three hours after a feeding. Another indication is the diarrhœa and vomiting which affects infants recently put upon artificial feeding. Contraindications to lavage are collapse, inflammations of the respiratory passages, laryngitis stridulus, eclampsia, and tetany.—*Fortschritt der Medicin*, 1904, No. 18, p. 767.

An Antitoxic Treatment of Tuberculosis.—Dr. E. Wahlen concludes a paper upon this subject thus: The treatment of tuberculosis by tuberculous iodonuclein gives brilliant results when administered at the beginning of the formation of anatomical lesions. If the invasion of the tissues has not been present more than a few months an *apparent* cure may be achieved. From six to twelve injections will accomplish this result. In advanced tuberculosis, where surgical ablation of the diseased tissues is impossible, the recent lesions are unaffected; however, in such cases the resisting powers of the organism are not sufficient to withstand the effects of so active a treatment. The author injects a solution which contains to each fifteen minims: nuclein, $\frac{5}{100}$ of a milligram; iodine, $\frac{1}{1000}$ of a milligram; potassium iodide and sodium borate, of each, $\frac{2}{1000}$ of a milligram. The dose for an adult is 5 minims at first, gradually increased to 20; for an infant 1, gradually increased to 10 minims. The injections are painful, but produce no inflammatory reaction.—*Gazette médicale de Paris*, 1904, No. 29, p. 338.

Intrapulmonary Infusions.—Dr. Rosenheim advises the following method of procedure: The pharynx and larynx are cocainized, and a tube, through which are injected several cubic centimetres of 2 per cent. eucaine solution mixed with a few drops of 1:1000 adrenalin chloride, is introduced into the trachea. Thus a tube may be passed into a bronchus without provoking a reflex act. Cough appears at the moment that the eucaine is injected, but lasts but a moment. If there is tendency to hæmoptysis the procedure is contraindicated. Through the tube introduced into the bronchus five to seven drachms of 0.01 per cent. tuberculin solution are injected. The injection is repeated in three or four days, and if no reaction is observed the strength of the solution is

increased gradually to 0.1 per cent. The tube is of small calibre, and about sixteen inches long. The patient should breathe deeply during the operation and for some time afterward if the solution is to reach the apex of the lung. Dr. Jacob reports that five patients at the beginning of the second stage of the disease, who had been ill for about a year and were much emaciated, to whom from fifteen to forty treatments had been given during from three to six months, were much improved. From four to eight weeks after the beginning of the treatment the bacilli disappeared, the body weight was increased, and a considerable diminution in the extent of the physical signs was noted. —*Revue de thérapeutique*, 1904, No. 15, p. 526.

Adrenalin in Cancer of the Upper Respiratory Passages.—M. Ichard observes that topical applications of adrenalin, while they may not effect a cure, sensibly diminish the pain and tendency to hemorrhage of epitheliomata. He has obtained especially good results in cancers of the pharynx and larynx. In certain cases an almost complete cicatrization has been brought about, which in one patient lasted ten months. The 1:1000 solution was first employed, but on account of its deterioration upon standing the following formula was advised: Adrenalin, 5 parts; tartaric acid, 5 parts; sodium chloride, 90 parts; 0.15 of a grain of this powder added to ten drops of water. The author recommends applications of the solution thus made every two days. Not only cancers of the larynx and tongue were benefited by the treatment, but also those of other regions, including the breast.—*Revue francaise de médecine et de chirurgie*, 1904, No. 31, p. 741.

The Bloodless Treatment of Furunculosis.—Dr. Sembritzski has employed the following treatment in a series of cases, some of which were very severe, with excellent results: First the skin is cleansed with ether and shaved, then the entire inflammatory area is covered with a wet gauze dressing of absolute alcohol and hermetically sealed. As an adjunct to the treatment the patient is given beer yeast or some one of its derivatives, such as "zyma." The dose of the former is a tablespoonful three times a day; of the latter a teaspoonful. These are given in water or beer. In twenty-four hours the dressing is removed, and in favorable cases the swelling, redness, and œdema will be found much diminished. In such cases the treatment is continued, but unless an amelioration takes place within the first twenty-four hours the use of the knife is indicated.—*Wiener klinische therapeutische Wochenschrift*, 1904, No. 29, p. 781.

The Treatment of Insomnia of Cardiac Origin.—L. Feilchenfeld advises in the insomnia which is present in certain cases the use of the following heart tonic: One-fifth of a grain of powdered digitalis leaves are mixed with one-thirtieth of a grain of morphine hydrochlorate, and the powder is taken at bedtime. The author believes that this insomnia, which is characterized by a slumber of an hour or two early in the night, followed by wakefulness accompanied by weariness, oppression, and palpitation, is due to cardiac insufficiency and passive dilatation. The small dosage recommended is usually sufficient to give relief, and no unpleasant after-effects, such as may follow larger doses, are noted.—*Journal de médecine de Paris*, 1904, No. 28, p. 280.

The Treatment of Aneurysms of the Aorta by Injection of Gelatin.—Dr. Lancereaux has injected the following solution subcutaneously, with the best of results: distilled water, 1000; sodium chloride, 7; gelatin, 25 parts. The gelatin must be of the best quality, and the solution should be sterilized several times under pressure at a temperature of 110° to 115° C. Each injection consists of about six ounces, and the treatment is repeated every four or five days. The procedure causes a cessation of the pain and a hardening and shrinkage of the sac. The patient may return to work, provided he avoid exertion. The author concludes thus: The method is not dangerous, provided the gelatin be pure and thoroughly sterilized. The injections favor the coagulability of the blood in the aneurysmal sac, and thus tend to cure. Tetanus or other complications are always due to poor gelatin or lack of sterilization.—*Gazette médicale de Paris*, 1904, No. 28, p. 328.

The Alkalies in Diabetic Coma.—Dr. Lenne reports a case which after having been affected for two years with diabetes suffered a typical attack of coma. In addition to alcoholic stimulation a solution of a mixture of two and a quarter ounces of sodium bicarbonate and one ounce of magnesium carbonate was administered. The patient gradually recovered until in three days all signs of the coma had disappeared. Shortly afterward he suffered a second attack, which was also controlled, but larger quantities of the alkalies were given. This case is in direct contrast to three similar cases in which the alkaline treatment had no effect.—*Deutsche Aerzte-zeitung*, 1904, No. 8, p. 180.

Validol and Seasickness—Dr. K. Koepke has found that in the early stages of seasickness 10 to 15 drops of validol upon a lump of sugar, with advice to lie down for half an hour, at the end of which a glass of wine and a biscuit may be taken, is sufficient to prevent further symptoms. In more marked cases which have been prostrated by a day's *mal de mer* the patient should be put to bed and given validol on sugar as above. After half an hour the yolks of two eggs, mixed with sherry and ice, are given by teaspoonful; without exception this will be found to be well borne. After this procedure has been carried out several times in the course of the day, the patient may be allowed light diet. —*Therapeutische Monatshefte*, 1904, No. 6, p. 296.

The Action of Strophanthus.—Dr. G. Günther, after an examination into the action of this drug upon horses, sheep, dogs, and other smaller animals, has arrived at the following conclusions: 1. Strophanthus is purely a heart muscle poison in mammals, and produces death by causing stoppage of the heart in diastole. 2. In poisonous doses it causes characteristic changes in the pulse and blood pressure, different from those caused by digitalis through the absence of stimulation of the vagus. 3. Strophanthus is a vasoconstrictor, but is less active in this regard than digitalis; this action is, however, not marked in overdosage. 4. Strophanthus possesses a specific action upon the vomiting centre. 5. Of antidotes the chief place is occupied by artificial respiration. Excitants are without influence, as they are in poisoning by morphine and chloral hydrate.—*Therapeutische Monatshefte*, 1904, No. 6, p. 285.

OBSTETRICS.

UNDER THE CHARGE OF

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Ovarian Tumors during Pregnancy and the Puerperal Period.—Lea (*Journal of Obstetrics and Gynecology of the British Empire*, August, 1904) contributes a paper upon this subject, reporting four cases. He quotes the frequency of ovarian tumors during pregnancy as 5 in 17,832; Flaischlen, 2 in 1300; Lohlein, 1 in 1738; Tarnier, concluding that 1 in 2500 is the average frequency. At St. Bartholomew's Hospital Cripps had 2 cases in 182 patients with ovarian tumors.

Dermoids are more frequent in the proportion of 4 out of 7, about 25 per cent. Torsion of the pedicle occurs in from 6 to 12 per cent. during pregnancy, and during the puerperal period in about 22 per cent. Rupture is found in from 3 to 4 per cent. In Lea's 4 cases torsion occurred in 2; necrosis of the cyst followed by rupture and peritonitis during the last month of pregnancy occurred in 1, and impaction of a dermoid cyst in 1 case. In 12.5 per cent. Williams found that pregnancy was interrupted by the presence of the tumor.

The prognosis, so far as death is concerned, in these cases is fairly good. In 461 cases Williams found only 1 of sudden death from rupture, and 6 in which the tumor ruptured during pregnancy, when the patients died after labor. Labor and the puerperal period greatly increase the danger and bring the total mortality up to 25 per cent.

Regarding treatment, patients without operation show a mortality of 21 per cent.

Lea describes the case of a woman, aged forty-two years, in her sixth pregnancy at eight and one-half months. She had been in bed for six weeks, with severe abdominal pain and nausea. She had slight jaundice. Her temperature was from 100° to 101°; her pulse 120 and weak. The pelvis was occupied by a fixed tumor preventing the engagement of the head. Operation was done through the vagina, and a necrotic cyst adherent to the anterior wall of the rectum was removed in fragments. The pedicle was recognized and ligatured. The patient collapsed, but rallied with saline transfusion. Labor was spontaneous twenty-four hours later, a living child being born. The patient recovered, but died six months afterward from myelitis.

When an ovarian tumor obstructs labor its removal is imperative before an effort is made to deliver the child. In fifteen cases of ovariotomy during labor all recovered. In cases otherwise treated the mortality rose to nearly 50 per cent.

During the puerperal period ovarian tumors are dangerous through torsion of the pedicle, peritonitis, and suppuration, and necrosis in the cyst. Cysts often become infected when general septicæmia develops.

Lea reports the case of a woman delivered spontaneously of a living child who four days later had all the symptoms of puerperal infection. A hard mass of exudate in Douglas' pouch was found pushing the uterus forward. In performing posterior vaginal section a large quantity of pus was evacuated and a drainage tube inserted. The patient recovered.

Five years later she was again delivered of a living child in natural labor. On the third day infection developed, and a tumor the size of a large orange was found behind the uterus. On posterior vaginal section the tumor was readily exposed, adhesions broken up, the pedicle tied with silk, and the tumor removed. It was a dermoid of the left ovary. The pelvic cavity was flushed and packed with gauze, the patient making a good recovery. No organisms were discovered in the tumor or fluid. Without operation the post-partum mortality of these cases is about 28 per cent. In operation during the puerperal period a mortality of 14 per cent. is reported.

Post-partum ovariotomy is often remarkably successful. McKerron collected 92 cases with 79 recoveries—a mortality of 14 per cent. In 2 of these cases gangrene was present, and in 2 cases the tumor was malignant. From twenty-four to forty-eight hours after delivery is the most favorable time for this operation.

The Automatic Action of the Uterus and the Effect of Drugs upon Uterine Contractions.—In the *Archiv für Gynäkologie,* 1904, Band lxxiii., Heft 2, KURDINOWSKY reports the results of experiments made in the pharmaceutical laboratory of Professor Krawkow at St. Petersburg. Under ether the uterus of a rabbit was removed and placed in a neutral fluid at a temperature of 38° C. The whole was placed in a warm, moist chamber. Ludwig's kymographion was used to study the uterine contractions.

Immediately after removal from the body the uterus seemed relaxed. In about half an hour automatic contractions began earlier in the pregnant than in the non-pregnant uterus. The tissues of the uterus and vagina contracted separately, the uterus after an hour becoming apparently fatigued, and after an hour's rest again contracting. The uterine muscles began to act at the cornu, peristalsis continuing through the uterus to the vagina. To continue the experiment the temperature at which the uterus was kept was reduced three or four degrees, when it was found that contractions of the uterus persisted and could be excited in one case forty-nine hours and forty minutes after the removal of the womb from the body of the animal.

When this action of the uterus was studied it was observed that the muscle began its work at each cornu in alternation. The effect of this would be to force a body like the ovum downward into the uterine cavity. When the uterus had accomplished this the broad ligaments contracted in a direction transverse to the long axis of the womb. This action lasted but for a certain time, and when the ovum reached the vagina the broad ligaments ceased to contract. Each half of the uterus and broad ligament acted independently of the other, but in alternation. This action was entirely automatic and absolutely without the influence of the central nervous system.

In experimenting upon the pregnant uterus it was found that if blood were entirely washed out of the womb by injecting salt solution the ovum

died as soon as the womb became anæmic. The contraction of the uterine muscle, however, continued for fifty minutes after the uterus had been deprived of blood. For thirty-five minutes of this time the uterus was without the body of the mother. It was found that hot and cold stimulated uterine contraction to an equal degree. Variations in temperature seemed more stimulating than either heat or cold. At the usual termination of pregnancy the uterus is in a condition automatically to expel the fœtus.

In experimenting with drugs upon uterine contraction hydrastis, canadensis, ergot, chloral hydrate, and adrenalin were employed.

Hydrastin produced tetanic contraction of the uterine muscle, but did not affect the bloodvessels of the uterus. Ergot and its preparations had the same effect that hydrastin had on the uterus. Narcotics, as chloral hydrate and alcohol, had little effect upon the uterine muscle. When given to the point of narcosis their action became apparent.

Adrenalin in very weak solution produced marked effect upon the womb. In 1:10,000,000 it considerably increased the strength of uterine contractions. If pushed to any extent it produced well-marked tetanus of the uterine muscle. It produced an extraordinary vigorous effect upon the vessels of the uterus, causing them to contract. Experiments upon living animals confirmed those made upon the exsected uterus.

The Prevention of Morbidity during the Puerperal Period.—KROEMER (*Monatsschrift für Geburtshülfe und Gynäkologie*, 1904, Band xx., Heft 2) draws attention to the value of taking all possible precautions to prevent complications during the puerperal period. During 1893, in the Marburg Clinic, the percentage of morbidity was 38.7. Severe infections occurred in 1.07 per cent., while the mortality from septic infection was nothing.

In preventing complications during the puerperal period the introduction of rubber gloves had unexpectedly been without result. It must be remembered that even in healthy patients the vagina contains germs capable under some conditions of becoming actively pathogenic. For this reason, although with rubber gloves, the hand may be practically sterile, its use cannot entirely remove causes of puerperal infection. The effort to destroy these germs by vaginal douching and cleansing exposes the patient to such danger of uterine infection as to be undesirable. Furthermore, in from 20 to 22 per cent. of pregnant patients the secretion of the vagina is pathological in character.

As regards labor itself, patients admitted to the clinic with fever are confined in rooms set apart for such cases. If a patient, already in the house, develops fever during labor the confinement-room is immediately disinfected. Every precaution is taken to at once stamp out the infection. Except in infected and suspicious cases the use of gloves is not insisted upon, nor considered of practical value.

In the lying-in ward all who have to do with the care of patients are required to use gloves. Douches are given during the first two or three days, and nurses use sterilized forceps to handle cotton sponges and other dressings. Every precaution is taken to avoid the spread of contagion from one patient to another. Cases developing fever are at once isolated.

When patients are received and examined before labor the entire body is thoroughly examined, and in addition the character of the

vaginal secretion is ascertained. When this is pathological and abnormal a vaginal douche of 1:2000 bichloride is used. If gonorrhœa is present rheol, followed by a douche of lysol ½ per cent., are used. All pregnant patients are examined twice weekly, and the genital region thoroughly explored to detect ulceration or signs of infection. The legs are examined for varicose veins or ulcers. Patients are obliged to bathe daily, and strict precautions are taken about linen.

The breasts are inspected, the nipples thoroughly washed, and alcohol used with glycerin and boric acid for local antisepsis. The danger of erysipelas arising from excoriation of the nipple is considered great, and every precaution taken to avoid this accident. Areas of distention caused by the accumulation of milk do not produce serious consequences.

In choosing antiseptics for douches care should be taken to employ dilute solutions to avoid irritation and injury. With such precautions the morbidity percentage of several clinics shows about 30 in operative cases and less than 15 in cases of spontaneous parturition. It is considered of especial importance that pregnant patients be kept under complete and absolute control and that the reduction of complications in labor and the puerperal state will depend upon the thoroughness and perfection of this precaution.

GYNECOLOGY.

UNDER THE CHARGE OF

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Leukocytosis in Gynecology.—PANKOW (*Zentralblatt für Gynäkologie*, 1904, No. 11) states that in all cases in which there is a persistent leukocytosis of over 10,000 (without any other satisfactory explanation) the presence of pus in the pelvis should be inferred. It cannot always be excluded with a lower count, since there may be either a tuberculous focus, or the abscess may be surrounded with such dense adhesions that no absorption occurs. Hæmatoceles, so long as they do not suppurate, are unaccompanied by leukocytosis. A post-hemorrhagic leukocytosis may, however, follow rupture of a tubal gestation.

Torsion of the pedicle of an ovarian cyst is rapidly followed by an increase in the white cells, possibly due to the accompanying irritation of the peritoneum, but in acute peritonitis this may be absent, as the power of reaction of the system is increased. Leukocytosis, from 11,000 to 13,000, is a more reliable indication of pus than the temperature curve (?).

In cases of cancer no inference can be drawn from leukocytosis with regard to the locality, character, or extent of the disease. Even when

necrosis is present (unless there is actual pyometra) there is no increase in the white cells, probably because the sloughs are rapidly cast off and there is little absorption. No increase is observed when the lymph nodes are affected. Among the cases of fibromyoma which were studied with especial reference to leukocytosis, this was noted in only a single instance as a post-hemorrhagic phenomenon.

After the evacuation of abscesses by colpotomy a diminution in the number of leukocytes was promptly noted, unless pus-foci were not thoroughly drained. After abdominal section in pus cases there was at first a marked increase, which gradually declined to the normal if the case progressed smoothly. Imperfect drainage, mural abscess, etc., caused a fresh increase in the number of leukocytes. Even in aseptic cases the same degree of leukocytosis was noted on the first day after operation, although there might be no accompanying elevation of temperature. The writer explains this phenomenon on the theory that in every operation, no matter how aseptic, a certain amount of infectious material is introduced into the wound, the absorption of which into the circulation produces a marked irritation of the leukocytes.

Further observations during normal pregnancy and labor led the writer to the following conclusions: Leukocytosis is seldom found at the end of pregnancy. There is an increase during labor, most marked if the pains are severe and the labor prolonged. The maximum is reached an hour or two after the completion of the third stage. There is a gradual decline to normal on the fourth day.

The Uterus in Ectopic Gestation.—Cazeaux (*Revue prat. d'obstétrique et de pediatrie*, November, 1903) finds that in ectopic gestation the uterine mucosa is intensely congested and hypertrophied, interstitial hemorrhages being frequent. This explains why the passage of the curette usually causes bleeding. The pseudomembrane is rarely expelled in the shape of casts of the uterine cavity, the shreds being more often overlooked in the accompanying blood. This usually occurs early in the pregnancy, and does not by any means imply the death of the product of conception, but it is usually indicative of rupture or tubal abortion.

Cancerous Degeneration of the Cervix after Supravaginal Amputation.—Richelot (*Annales de gyn. et d'obstétrique*, December, 1903) concludes a paper on this subject with a positive expression of his preference for pan-hysterectomy in cases of fibroid where a radical operation is indicated.

He also believes that fibromyomata are only relatively benign. While, of course, it is not always necessary to remove them, he has seen too many patients with these neoplasms succumb to phlebitis or visceral disease, while under observation, to regard them as entirely innocent. While sarcomatous degeneration is rare, he does believe that cancer frequently develops in fibroid uteri in consequence of the accompanying endometritis. He cites two cases from his own practice and ten from the literature in which the cervix became cancerous after supravaginal amputation.

Obliteration of the Tubes.—Ronsse (*Annales de gyn. et d'obstétrique*, December, 1903), from experiments on animals, concludes that the

lumen of the tube can be completely obliterated by section between ligatures. He obtained the same results in six operations upon the human subject, and prefers this method to the more complicated ones that have been proposed. It cannot be denied that there is always a certain amount of risk of subsequent dilatation of the tube, so that the operation should not be resorted to unless it is clearly indicated, as after Cæsarean section, in tuberculous and cardiac cases, etc.

The writer criticises the operation proposed by Kehrer as liable to abuse and not free from danger.

Histology of Chronic Oophoritis.—PINTO (*Zentralblatt für Gynäkologie*, No. 23, 1904), after reviewing the various conflicting views with regard to the inflammatory nature of this affection, states the conclusions to which his own histological studies have led him. He objects to the division into interstitial and parenchymatous oöphoritis, because it is hardly possible to separate the two varieties, even in the acute form. Since in some cases the cortical layer is first affected by contiguity, and in others the deeper portions of the ovary are primarily infected through the medium of the bloodvessels and lymphvessels, he suggests the terms "cortical" and "diffuse" oöphoritis. In the former the albuginea is thickened, partly from adhesions, the ovary being usually of nearly normal size; and, if the case is not of long standing, round-cell infiltration will be observed in the neighborhood of the vessels. Later portions of the stroma will be converted into firm fibrous tissue, containing islands of normal tissue with a few primary follicles. In the latter atrophy of the nuclei and degeneration of the protoplasm will be seen, especially in the more superficial follicles. They are not increased in number, and in some the epithelium and ovum may be practically unchanged.

In the diffuse variety the ovary is cirrhotic, with hyperplasia of the stroma and a diminution of the number of follicles, which, however, are normal or exhibit a tendency to atresia or cystic degeneration. The vessels show hyaline degeneration of the middle layer of the intima, obliterating endarteritis, or perivascular sclerosis. Round-cell infiltration is rare, but hemorrhagic foci are seen, both in the stroma and in the follicles. The appearances correspond to those usually described as interstitial oöphoritis, which may result in general sclerosis. The writer dissents from the opinions expressed by Martin and Orthmann, that cystic degeneration of the ovary is necessarily the result of a chronic inflammatory process in or around the ovary. As regards etiology, he believes that infection (gonorrhœal or septic) plays the principal role, though chronic congestion from any cause may act as a predisposing factor.

Changes in the Uterus in Ectopic Gestation.—CAZEAUX (*Revue prat. d'obstét. et de pediatrie*, 1903, No. 11) says that in connection with tubal pregnancy the uterus is gradually pushed forward and to one side. If many adhesions are present it may be impossible to map out the body of the organ. The cervix remains softened, he affirms, as long as the product of conception is living, though this softening is not so marked as in normal pregnancy. The same applies to the corpus uteri, which becomes notably smaller and harder after the death of the fœtus. The writer differs from some authorities in holding that pseudomembrane

may be cast off from the uterine cavity at any time during the extra-uterine pregnancy and that it does not necessarily point to the death of the fœtus, though it is often significant of hemorrhage into the tube or tubal abortion.

Adenoma of the Fallopian Tube.—NADORY (*Zentralblatt für Gynäkologie*, 1904, No. 23) reports the following cases:

Case I. A II-para, aged twenty-eight years, had suffered for three weeks with abdominal pains and a bloody discharge. A diagnosis of incomplete abortion with enlargement of the left tube was made, and the uterus was curetted. As the tube did not diminish in size under treatment and the patient continued to suffer great pain, laparotomy was performed. A pus-tube was removed, which was thought to be tuberculous, but on microscopic examination it proved to be a typical adenoma.

Case II. The patient, aged twenty-nine years, had been sterile for eight years, and was sent to the clinic as a case of probable ruptured ectopic gestation. On opening the abdomen general adhesions were found, the affected tube was removed, and showed at its isthmus a myoadenoma, such as was originally described by Recklinghausen, the mucosa being intact. The writer regards this obstruction of the lumen as the cause of the tubal pregnancy.

Extirpation of the Spleen.—CASATI (*Zentralblatt für Gynäkologie*, 1904, No. 23) reports five cases, in three of which the spleen was enlarged from malaria, once from cancer, while there was one case of idiopathic enlargement. The patients all recovered, those with the malarial spleens being cured. The writer does not advise splenectomy for this cause unless the tumor has reached a very large size. He makes a medium incision and uses a Mikulicz drain if extensive adhesions have been separated.

Metrorrhagia in Syphilis.—OZENNE (*Soc. médico-chirurg. de Paris; La gynécologie*, June, 1904) calls attention to the fact that this symptom is generally observed during the tertiary stage, but that it may appear during the secondary, and may be of diagnostic value in the absence of local evidences of infection. He reports two cases which yielded to mercurial treatment after all local measures had failed.

Drainage after Laparotomy.—SCHWEIZER (Inaugural Dis.; abstract in *Zentralblatt für Gynäkologie*, 1904, No. 23), from an analysis of a series of cases at the Zurich clinic in which drainage was employed by means of gauze wrung out in sterile water, or a solution of salicylic acid, and brought through the lower angle of the wound, arrives at these conclusions: In cases in which there is doubt as to the sterility of the pus in a case of tubal or ovarian abscess, and when a perforation of the intestine has been sutured, the gauze drain or tampon should always be used, since in this way many fatal results can be averted.

[We have cited his paper in order to emphasize the expression "or tampon," since the writer, by stating the fact that gauze acts as a tampon, as well as a drain, involuntarily admits the weak point in his argument. He evidently has not followed the trend of modern surgical technique, which is that so-called gauze-drain (especially when it is

introduced through a small abdominal wound) more often prevents than favors the escape of fluid. In those exceptional cases in which gauze-tamponade of the pelvis is employed it is generally admitted that the vaginal route is the natural one for drainage.—H. C. C.]

OTOLOGY.

UNDER THE CHARGE OF

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Injuries of the Drumhead from Indirect Violence.—W. BOEHM (*Monatsschrift für Ohrenheilkunde*, March, 1904) states that injuries of the drumhead, in the form of a solution of its continuity, are more frequently the result of indirect violence than of puncture by foreign bodies, destruction by chemical action, or perforation as a consequence of extreme temperature limits locally applied. This is in accordance with the fact that even a very moderate degree of air pressure applied in such fashion as to force the drumhead to make a major excursion within a limited period of time is sufficient to ensure its rupture.

It is not the forceful box upon the ear which ruptures the drumhead so often as the less forcible blow with the flat of the hand covering the whole auricle, and, for a moment, making an air-tight closure of the canal; and it is interesting to note that the clinical records of cases of injury to the ear from this cause show the majority of them to have occurred on the left side, a natural result of the preponderance of right-handed blows.

That the condition of the drumhead itself should exert an influence upon the extent and location of the injury resulting from a sudden excursion under the influence of air pressure is evident, as illustrated in cases of partial atrophy of the drumhead, of cicatricial adhesions, or of the weighting of certain portions by the presence of calcareous deposits.

That detonation at short range may cause a rupture of one or both drumheads is not infrequently observed in artillery service, and the same is true in cases of dynamite blasters, in divers, and in caisson workers. Injury of the same character may also be caused under conditions of exhibition of pressure from within outward, by sudden compression of the air within the middle ear, as in violent coughing, sneezing, and vomiting, or by the use of the Politzer air douche and, contrariwise, by the sudden exhaustion of the air in the external canal, as in a case reported by Huettig, where a kiss upon the ear resulted in a rupture of the drumhead.

There is still another group of injuries to the drumhead, those resulting from cranial concussion, which has not, as yet, been sufficiently

classified, and which includes not only cases of simple contrecoup, but of double-sided injury as well.

Of these latter cases the author has found but one record in reviewing the literature of the subject, the case reported by Stankowsky, of a young man who had perforation of both drumheads as the result of a heavy blow upon the left ear, in which ear there was also a labyrinth concussion as further evidence of the force of the impact.

The exact mechanism of the injury by contrecoup is not yet adequately determined, and it is possible that help for solution of the general question may be reached through carefully collated records of injury to the drumhead and such observations as have been attempted by Corradi, who finds that the majority of solutions of continuity resulting from air pressure occur in that portion of the drumhead which is both the thinnest and the most movable, namely, the central portion, while the injuries as the result of contrecoup are, as a rule, longitudinal ruptures starting from some point at the periphery of the drumhead and running wholly or partly across it, a condition which he regards as consonant with the proposition that in the transference of motion from a medium of one density to that of another of different density, the point of transference is that at which the solution of continuity is most likely to occur.

With this opinion of Corradi the author does not, however, agree, holding that ruptures of this type are not the result of irradiation, and the transference of the force exerted to a weaker medium, but are exhibitions of the true contrecoup reaction.

This view is based upon the experiments of Bergmann and Messerer upon the elasticity of the bones of the skull, considered as parts of an elastic globe, with susceptibility to "bursting fracture" primarily at points at right angles to the line of compression, and, secondarily, where there is a simple blow without counteracting pressure, midway between the point of impact and the right angle above mentioned; in other words, the author holds that ruptures of the drumhead consequent upon blows upon the skull other than those directly applied to the affected ear are the result neither of compression nor of irradiation, in the sense of Corradi's theory, but of a true "bursting fracture" incident to the natural elasticity of the skull which makes the phenomenon of contrecoup possible.

The Surgical Treatment of Peripheral Paralysis of the Facial Nerve.—G. Alexander (*Archiv für Ohrenheilkunde*, Band lxii, Heft 1–2.) reports a case of grafting of the facial nerve to the hypoglossal. The patient presented complete left-sided paralysis of six years' duration, as the result of chronic suppurative middle-ear disease. The radical operation was performed and the labyrinth found diseased and filled with polypoid granulations. The facial and its canal were completely destroyed by the disease. Examination of the region supplied by the left facial showed the orbicularis oris somewhat contractile, but complete paralysis of the other face muscles and of the platysma. There was no disturbance of the taste sensation on the tongue, and there was a normal condition of the soft palate. Galvanic and faradic stimulation of the muscles by way of the nerve gave no reaction. However, direct faradic stimulation showed a slight reaction of the orbicularis oris of the under lip and direct galvanic stimulation showed evident reaction

of the orbicularis of the upper and under lip. The grafting of the facial and hypoglossal was accomplished by exposing the hypoglossal in the angle made by the two bellies of the digastric muscle, dissecting out the facial trunk where it emerges from the stylomastoid foramen, cutting this off obliquely (a small bit of the nerve taken from this end and subsequently examined microscopically showed complete degeneration of the nerve fibres), and then suturing this end to the side of the hypoglossal nerve after denuding a small area on the side of this nerve of its neurilemma.

Six weeks after the grafting, the condition was as follows: Indirect faradic stimulation gave no reaction. Indirect galvanic stimulation (the electrode was applied over the scar of operation) showed slight reaction of the orbicularis oculi and the orbicularis oris of the upper and under lip, also of the depressor anguli oris. Direct faradic stimulation showed reaction in the orbicularis oris of the under lip and direct galvanic stimulation showed slight reaction in the same muscles which responded to indirect galvanic stimulation.

Alexander reviews the cases of suture of the facial to the spinal accessory reported by Ballance and that of Faure, where the facial peripheral end was sutured to the proximal end of the completely separated hypoglossal. A case of Körte of grafting similar to Alexander's own case and a case of facial-spinal accessory suture by Glück are briefly reviewed. Three methods have been employed:

1. Grafting of the several facials to the spinal accessory.
2. End-to-end suture of the peripheral end of the severed facial to the proximal end of the severed hypoglossal.
3. Grafting of the severed facial-peripheral end to the hypoglossal.

Of these methods Alexander believes the third most desirable because, in the first method, there are associated movements of the shoulder; and in the second method, although an end-to-end suture gives the best chance for regeneration of the nerve fibres, a permanent one-sided paralysis of the tongue and a consequent atrophy of the paralyzed side results. In no case thus far observed has a complete restoration of the function of the facial resulted.

As to the time after the onset of the facial paralysis at which the grafting should be undertaken, Alexander believes:

1. The grafting of the facial should not be undertaken before six months after the time of the appearance of the paralysis, and during this time, massage and electric treatment should have been tried.
2. After six months all cases should be operated in which (*a*) no voluntary contraction has become possible; (*b*) in which no faradic excitability is present; (*c*) in which the galvanic excitability of the nerve, in spite of treatment, decreases.
3. In cases of more than six months' duration a favorable result of grafting can be expected only when there remains some direct galvanic excitability.
4. If, in old cases, there is prompt galvanic reaction or there is a remnant of faradic excitability, some conservative treatment for a time is indicated.

Middle-ear Disease in its Relation to Metastatic Abscess of the Liver and Other Viscera.—S. Macuen Smith (*Archives of Otology*, April, 1904) reports three interesting cases of metastatic abscess of the

liver of otitic origin. While almost all of the cases of abscess of the liver are due to such causes as dysentery, appendicitis, gastric ulcer, etc., he believes that the so-called cases of "spontaneous abscess" of the liver may be due to primary foci in the ear.

The first case is that of a man, aged forty-two years, who had suppurative disease of the middle ear for twenty-seven years. For the past twenty years he suffered no inconvenience beyond a slight discharge, with the exception that he has had increase in the amount at intervals for three years. The writer saw the patient during one of these attacks. After a chill the temperature registered 105.2°, followed by profuse sweating. He complained of severe pain in the right shoulder and neck, and a moderate yellow tinge of the skin was noticed. The aural examination showed a complete destruction of the membrana tympani, malleus, and incus. Pus was present in the canal, and was very offensive. Examination of the mastoid process and adjacent parts was negative. The severity of the above symptoms increased, and a week before death the liver was found to be enlarged. There was also pain in the hypochondrium. The temperature was pyæmic in character, and just before death registered 106°.

Antistreptococcic serum was used, but with no beneficial effect. At the autopsy all the organs were negative, except the liver, which was a mass of miliary abscesses.

A second case is reported similar to the first, with the exception that the duration was of eight years and the discharge was not so offensive. The autopsy revealed multiple abscesses in both the liver and lungs.

The last case is that of a man, aged twenty years, who had suppurative disease of the middle ear since an attack of measles when he was four years of age.

Previous to the present attack the ear had been dry for six months. Two days after the discharge began he complained of severe and constant pain in the vicinity of the right ear. Temperature at this time was 98°. Two days later the temperature rose and the pain increased. The mastoid was found to be tender, and an operation was performed at once. The bone was necrosed, and the cells filled with pus and granulations. No evidence of sinus involvement. Two days later the temperature rose to 104.4°, the dressing was removed, and the wound found to be very offensive; 30,000 units of anti-streptococcic serum were given. The next day a second operation was performed, the lateral sinus being opened and found to be thrombosed. This was curretted, and the temperature fell to 97°. Seven days after the second operation the patient had a chill, and the temperature rose to 105°. Chills occurred at different intervals for a week, when tenderness over the jugular vein being noticed, an incision was made and the vein found to be healthy. The patient complained of pain in the right shoulder and neck, and the liver was tender. Death occurred about a month after the onset of the disease. The autopsy revealed a mottled appearance of the brain at the seat of the mastoid operation. The lung, liver, and spleen showed many miliary abscesses. The heart and kidneys were negative.

The writer summarizes the most important features as follows:

1. Acute exacerbation of a chronic process—an early symptom.
2. The severe pain in the right shoulder and neck beginning at the same time as the hepatic suppuration.

3. Pain and tenderness of the right hypochondrium, indicating hepatic disease.

4. Repeated chills, pyrexia, and diaphoresis, indicating a septic process likely to prove fatal.

5. The marked accessions and remissions of temperature, typical of hepatic abscess.

6. While jaundice was a constant feature it was of little diagnostic value.

7. The conclusion drawn is that metastatic abscess of the viscera may be caused by suppurative disease of the middle ear.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

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Pelliculous Sore-throats.—The profession has long been aware of the existence of various pelliculous sore-throats which were not diphtheria, and these have caused considerable confusing controversy. Bacteriologic investigation is gradually differentiating these affections. One variety, now known as Vincent's angina, has been the subject of careful study during the latter half of the present decennial. An excellent summary of what is known about this form of pelliculous sore-throat has been written by Dr. Randle C. Rosenberger (*American Medicine*, July 23, 1904), who reports in addition two cases of Vincent's angina and one of noma in which the organisms characteristic of the former affection were found. Dr. Thomas H. Harris (*ibid.*), of New York, reports two cases, and discusses a differential diagnosis under the caption "Primary Ulceration of the Tonsil," together with some remarks on tonsillar ulceration in general. Dr. G. C. Crandall, of St. Louis (*Journal of the American Medical Association*, July 23, 1904), reported a case of Vincent's angina and stomatitis at the late meeting of the Section on Stomatology of the American Medical Association. The patient was a medical student in fairly good health, with throat, mouth, and teeth in good order. The affection began in the tonsil and palate, and extended to the gums in consequence of cleansing of the teeth by a dentist on the fourth day of the disease.

Adrenalin in Malignant Disease of the Throat.—Dr. Aimar Raoult, of Nancy, reports (*Revue hebdomadaire de laryngologie, d'otologie et de rhinologie*, Juillet, 1904) a case of a man, aged sixty-eight years, whose right tonsil had in great part been removed by excision. Subsequent developments evincing malignancy, treatment with applications of adrenalin hydrochlorate, 1:1000, were instituted. While almost complete elimination of the tumor was eventually accomplished under the action of the adrenalin, serious œdema of the entire region had been

produced, including the anterior and posterior pillars, the uvula, and a great portion of the soft palate, so that the applications of adrenalin had to be abandoned temporarily. The patient was lost sight of, but was found to have died a few weeks after cessation of the treatment.

Primary Tuberculous Growth of the Nasal Septum.—At a recent meeting of the Laryngological Society of London (*Journal of Laryngology, Rhinology and Otology*, August, 1904) Dr. Smurthwaite showed a microscopic slide from a growth removed from the anterior portion of the cartilaginous septum on the right side of a woman, aged thirty-five years. The tumor was bluish-white and very uneven in surface. It was readily removed with a Volkmann spoon. The cartilage was then scraped bare, and the surface rubbed thoroughly with lactic acid solution, 75 per cent. Three months after treatment there had been no signs of recurrence.

As shown in the slide, the nature of the growth was undoubtedly tuberculous, for, though no bacilli were found, a number of giant-cells were seen to be present.

Carcinoma of the Nose.—At the late meeting of the Laryngological Society of London (*Journal of Laryngology, Rhinology and Otology*, August, 1904) Dr. Felix Semon showed a case of papilliferous columnar-celled carcinoma of the nose in a young man, aged twenty-four years. The patient had been sent to Sir Felix in consequence of recurrences after removal of a cauliflower growth from the region of the left meatus, and which apparently sprung from the septum high up from beneath the cribriform plate. Examination of specimens of the original growth showing it to be a papilliferous columnar-celled carcinoma, by advice of Sir Felix Semon, Sir Victor Horsley performed a very radical operation, as follows: He first ligated the external carotid, then, after plugging the rhinopharyngeal cavity, he did a Rouge operation, and removed the greater part of the bony septum, the left middle turbinate, and the ethmoid on the left side up to the cribriform plate. The operation occupied nearly two hours, but so far as could be judged succeeded in completely removing the growth with a healthy area around it. The patient made an uninterrupted recovery, and there had been no recurrence.

Cancer of the Ethmoid.—Dr. Marcel Lermoyez (*Annales des maladies de l'oreille, du larynx*, etc., Juillet, 1904) reports a case of cancer of the ethmoid in a man, aged forty-five years, which he removed after external exposure by resecting not only the nasal process of the upper jaw, but also the nasal bone proper, except its anterior border and the nasal spine of the corresponding frontal bone. This enabled him to expose the ethmoid frontally, instead of obliquely, as when access is made by way of the orbit. The growth, which on inspection through the natural passages was supposed to be the size of a nut, was found to be larger than an egg. It occupied the entire ethmoid, extending in front of the *agger nasi*, where it would have been totally impossible to reach it by way of the natural passages. The tumor was easily removed with the large ethmoidal forceps of Luc, which permitted its extraction in large fragments without notable hemorrhage. As there were no prolongations, its total ablation was practicable. The patient made a

good recovery, and left the hospital on the seventeenth day able to resume his work. Three months later, when the patient was shown to the French Society of Otology and Laryngology, June 15th, the local condition was perfect, a cicatrix barely visible indicating the line of incision through the soft parts.

The Utilization of the Lower Lip in Rhinoplasty: A New Procedure.—Dr. Carl Beck, of New York, exhibited to the Surgical Section of the Academy of Medicine (*Medical News*, March 5, 1904) a woman, aged fifty-five years, in whom he utilized portions of the lower lip and chin for replacing lost tissues of the left side of the nose. The patient had been operated upon about three years previously with flaps taken from the forehead and cheek, which, though apparently successful at the time they were made, had disappeared in a recurrence by the end of a year. In the absence of available tissue in the vicinity of the area, Dr. Beck operated by taking a large flap from the left arm. Eighteen months later another recurrence was followed, with more extensive destruction; the mucous membrane of the left nasal passage being completely exposed. The defect was covered by a triangular flap from the lower lip. The details of the procedure are illustrated by a diagram and three photographs. The advantage of this procedure seemed to the operator to lie especially in the possibility of supplying a mucous membrane throughout the whole area of the defect so as to restore normal conditions as far as practicable.

Spontaneous Disappearance of an Obscure Ulceration in the Larynx.—At the late meeting of the Laryngological Society of London (*Journal of Laryngology, Rhinology and Otology*, August, 1904) Sir Felix Semon showed a case of obscure ulceration of the left vocal cord of nearly a year and a half standing in a gentleman, aged about sixty years, which had since disappeared spontaneously. The case had been shown as an extremely obscure one, and fully described at the December meeting, 1903, when the discussion revealed considerable differences of opinion. Since then the patient, after an attack of influenza, became extremely ill, so that his life was despaired of for a considerable time. He was again seen, after an interval of several months, at the beginning of May, when it was found that the chronic and troublesome ulceration, which had existed for so long a time, had spontaneously and completely disappeared, so that there only remained slight congestion and relaxation of the left vocal cord. The question as to the nature of the chronic ulceration is thus more obscure than ever.

[In the compiler's experience epithelioma, syphiloma, and even tuberculosis of the throat have been known to undergo spontaneous retrogression during severe attacks of influenza and likewise of erysipelas.]

Tumor of the Larynx: Successful Treatment by Roentgen Rays in Neoplasm of the Larynx.—Drs. A. Beclere and Paul Viollet (*Revue hebd. de laryngologie, d'otologie et de rhinologie*, Juillet 9, 1904) report an extensive case of a laryngeal tumor supposedly malignant, apparently cured—temporarily at least—in a man, aged fifty-one years, by daily exposure to the *x*-rays as frequently as practicable from December 1, 1903, to March 29, 1904. The sittings were of fifteen

minutes' duration for the first two months and ten minutes only during the last month. Intervals between the treatment were rendered necessary by inflammatory reaction in the skin of the neck, through which the rays were passed on alternate sides during the first few weeks, and subsequently on the diseased side only.

Reference is made to a case similarly treated with equal success by W. SCHEPPEGRELL, of New Orleans (*ibid.*, 1903, No. 11), and another by DR. MASSEI, of Nice (*ibid.*, No. 10, 1904). In none of these cases had there been any histological examinations to determine the nature of the growth.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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Studies on the Pathology and on the Etiology of Variola and Vaccinia.—From the Sears Pathological Laboratory, the Harvard Medical School; *Journal of Medical Research*, 1904, vol. xi., No. 1.

Councilman, Magrath, and Brinckerhoff describe the pathological anatomy and histology of variola, and find that the lesions of variola may be grouped under three heads: (*a*) Those which are specific and due to the presence of a parasite peculiar to the disease. (*b*) Lesions which are associated with the above, but are of indeterminate specificity. (*c*) Lesions which are caused by accessory etiological factors, among which the most important are bacteria.

(*a*) The specific lesion of variola is a focal degeneration of the stratified epithelium of the skin and of the mucous membranes of the soft palate, the pharynx, and the œsophagus. The typical lesion is best seen in the skin. It makes its appearance on about the fourth day of the disease, and, passing through progressive stages, reaches its climax of development on the eighth or ninth day. It begins with degeneration of the cells of the lower layers of the epidermis and is accompanied by exudation, at first serous, but later more or less cellular. The final stage produces the filled-out pustule. This development may take place wholly within the epidermis, or the corium may form the base of the pustule. The subsidence and repair of the lesion is accompanied by the removal of the fluid portion of the exudate by absorption, by drying, and by the regeneration of the epidermis. During this process the mass of degenerated epithelial cells, leukocytes, debris, etc., is exfoliated. Associated with the lesions of the epidermis may occur œdema, cellular infiltration, and hemorrhage of the corium. The changes in the mucous membranes are like those in the skin, except that in the absence of the horny layer the degenerated epithelial cells are cast off and the vesicle is rarely seen; the pustule never.

Within these lesions of the skin and mucous membranes is found the parasite peculiar to variola. In its younger stages or cytoplasmic form it is found within the protoplasm of the epithelial cells, usually in the earliest lesions. The intranuclear form of the parasite is present for the most part in the more advanced lesions. Variations from that form of the disease which presents typical specific lesions are determined by differences in the character and extent of the lesion.

(*b*) The associated lesions consist of a proliferation of cells in the hæmopoietic organs, in the formation of mononuclear basophilic cells in the spleen, lymph nodes, and bone-marrow, and of phagocytic endothelioid cells in the lymph nodes and marrow. Focal and interstitial infiltrations of mononuclear basophilic cells are found in the testicle, liver, kidney, and adrenal glands. In the testicle are seen anæmic focal necroses, lesions which seem to be specific. Degenerations, focal in character, are found in the blood-forming cells of the bone-marrow. Diffuse toxic degenerations occur in the liver, kidney, adrenal glands, and testicle. The paucity of polynuclear leukocytes in the specific lesions, and the focal degenerations of the bone-marrow are strikingly peculiar to the disease.

(*c*) As a result of the action of pyogenic bacteria, acute degenerations are found in the parenchymatous organs. Boils, erysipelas, and cellulitis are common sequelæ, while pharyngitis and consequent bronchopneumonia are common in severe cases, often resulting in death. Lobar pneumonia, abscess, and gangrene of the lung occasionally occur, while endocarditis, pleuritis, and empyema are relatively rare. Acute lymph noditis is present in all severe cases.

In an elaborate article Calkins describes the organism discovered by Councilman and his coworkers in the specific skin lesion of variola, and discusses its life-cycle from a morphological study. The earliest stage is the extranuclear, a cycle which exactly corresponds to the observed life-cycle of the cytorrhyctes vaccinæ. The organism is first seen in the cytoplasm of the cells of the skin as spherical homogeneous minute bodies, which are interpreted as gemmules coming from sporulation ("multiple reproduction") of the organisms of primary infection. These bodies are seen to grow, first showing vacuolization in the centre and the occasional appearance of a minute central dot. Spore-forming material, for which Calkins suggests the name "protogonoplasm," is seen to be differentiated from the rest of the organism and becomes distributed throughout the body of the organism in the form of minute spherical granules. These granules become more and more definite in the later stages of growth, and are finally liberated by disintegration of the framework of the organism, which remains as a residual structure in the host cell.

The collections of protogonoplasm or gemmules thus liberated may either infect other cells as cytoplasmic organisms, or, ultimately, may become germ cells within the nucleus. In the latter case they develop into structures which the author regards as gametocytes or sexual forms, the products of which probably conjugate, as there are intranuclear amœboid bodies which are considered as fertilized female gametocytes or zygotes. This form is the first one seen to resemble a typical cell. It becomes the pan-sporoblast and the mother cell of the primary sporoblast.

Only one sporoblast is formed by the adult intranuclear parasite of

variola. The protogonoplasm which might be called the nucleus becomes distributed by fragmentation throughout the substance of the organism, the nuclear membrane of the host cell disintegrates, and these granules of protogonoplasm escape as spores apparently by the death and disintegration of the parent organism. The spores which are liberated from the pan-sporoblast are very minute, and are characterized by the presence of a vacuole which occupies the greater part of its mass, and a thickened portion at one side. Those which find their way into the nuclei of other host cells form secondary sporoblasts by a process differing from the pan-sporoblast formation. The thickened portion at one side of the spore ultimately extends around the vacuole or vesicle, and minute vacuoles appear in it. The sporoblast becomes a mass of vesicles which determine the seats of the formation of spores that are apparently identical with those formed by the primary sporoblasts.

This secondary sporoblast becomes free in the cytoplasm of the host cell by disintegration of the nucleus. Later the cytoplasm also disintegrates, leaving the sporoblast in the more or less broken-down substance at the bottom of the pustule.

There is a characteristic sporoblast residuum after both primary and secondary sporulation.

In a study "On the Occurrence of Cytocytes Variolæ (Guarnieri) in the Skin of the Monkey Inoculated with Variola Virus," Magrath and Brinckerhoff find skin lesions comparable to those in variola vera of man. In the epithelial cells of these lesions certain structures are seen which are identical in form and in staining reaction with those in the lesions of smallpox in man. The entire developmental cycle of the parasite can be followed through both the cytoplasmic and intranuclear stages.

To determine the etiology and pathology of vaccinia, experiments were made by Tyzzer upon rabbits, calves, sheep, and adult cows. Inoculations were made in the skin, mucous membrane, and particularly the corneæ. The work was extensively controlled by inoculations of pyogenic bacteria, diphtheria toxins, and many other substances. Successful vaccinations were obtained with vaccine lymph, active vaccine virus, and human variola virus. Inoculation of the blood from smallpox patients gave uniformly negative results. In all the lesions produced by these experimental vaccinations, either from vaccine virus or human variola virus, it is possible to demonstrate cell inclusions which are specific to vaccinia and which possess a definite and constant morphology. The vaccine bodies, first claimed by Guarnieri to be intracellular parasites, are closely related in their various types, and form a series which bears a definite relation to the development of the pathological process in which they are found. The epithelial cells are first invaded by small forms in which it is difficult to distinguish structure. Becoming located near the nucleus they grow larger, and it is then possible to make out a reticular protoplasm in which is a clear spot containing a mass of basic-staining material. It seems probable that the clear spot is a nucleus, and that the granule represents the chromatin of the organism. This chromatin mass later becomes irregular and eventually divides into a number of small granules, which constitute the small infecting forms of the organism. The above series of changes was never seen in any of the epithelial cells of the lesions

produced by the control experiments, and the author is convinced that the vaccine body is an organism and represents the etiological agent in vaccinia.

Brinckerhoff and Bancroft, from their studies on the leukocyte reaction in variola, conclude that a greater or less degree of leukocytosis occurs in all cases. The typical case of severe variola which recovers without complications presents at the beginning of the eruption a normal to subnormal count, which increases with the development of the cutaneous lesions, then suffers a slight decline, rises again during the latter stages of eruption, and, finally, falls to normal during convalescence. In fatal cases the count may be high during the early stages of eruption, but from then until death steadily falls. On the other hand, in mild cases there may be no rise above the upper limit of normal, or a gradually increasing leukocytosis, reaching its acme after the skin lesions have passed their active stage. Both primary and secondary types show a marked hyperleukocytosis. The leukocyte picture is characterized by an increase in the mononuclear cell types, though the minor variations in the leukocyte curves are dependent upon fluctuations in the absolute number of polymorphonuclear neutrophiles.

Southord finds that in variola the nervous system does not present any very specific lesions. Sections of the brain and cord from cases of variola in man and of variola inoculata in the ape stained by Nissl's, Weigert's, and the Marchi methods showed no characteristic degenerations, and the only finding in the nervous system which could be regarded as an essential part of variola is the hemorrhagic tendency sometimes seen in the cortex and cord in variola hæmorrhagica.

From a clinical and experimental study of the bacteriolytic complement of the blood serum in variola, Thompson concludes that in the early stages there is a diminution in the complement of the blood, but a rapid return to normal is seen in cases unattended with secondary infection. Cases in which there is a secondary infection show a failure of the complement-content of the blood to return to normal, while a progressive continued diminution in the complement-content is seen when the case is complicated by a terminal septicæmia. It therefore seems probable that the specific contagion of variola causes a diminution of the bacteriolytic complement of the blood. If the patient is capable of resisting the contagion the complement rises, but if the infection is particularly severe, or if for some other reason the complement does not rise, the individual, as he enters the pustular stage, immediately becomes susceptible to a secondary infection by the streptococci which abound in the later skin lesions.

Macacus and Rhoesus monkeys were found by Magrath and Brinckerhoff to be susceptible to variola inoculata, the disease pursuing a typical course with more or less constitutional reaction and fever. There are lesions of the skin consisting ordinarily of a primary pock at the site of inoculation, sometimes with local secondary lesions, and less commonly with associated general exanthem. The leukocytic equilibrium is disturbed, there being a polymorphonuclear, followed by a mononuclear, leukocytosis. The disease produced in the monkey by inoculation with variola virus is not identical with variola vera in man, but agrees with variola inoculata in man.

Within the epithelial cells of the epidermis and of the hair follicles at the site of the lesions cytorrhyctes variolæ may be seen. Successful

inoculation with variola was found to confer immunity to subsequent inoculation with both variola and vaccinia. Different strains of virus from different epidemics exhibited different degrees of virulence for the monkey, those coming from epidemics of clinically severe variola producing more severe lesions and being more likely to be followed by a general eruption.

In one case the variola virus was transferred from man to monkey, from the monkey to the rabbit's cornea through four generations, and when thus inoculated on a monkey produced a protopustule followed by a general exanthem.

T. R. Bancroft reports the clinical observations on variola, his paper being based upon the study of about 1200 cases. The symptoms of onset, the eruption and temperature are discussed at some length, and the disorders of the various systems and complications of variola vera are described. The abortive forms, including that which is generally designated "varioloid," are briefly discussed.

The second interesting class, variola sine eruptione, of which 12 cases were seen in physicians and attendants, consists of an indefinite illness marked by headache, pain in the back, fever, and nausea. It is a symptom-complex which appears twelve days after exposure to variola vera, and which usually lasts about three days. After the subsidence of the fever a few definite pocks occasionally appear. The author shows sufficient evidence to warrant the belief that true smallpox may arise from contact with such patients.

The very fatal variola hæmorrhagica is divided into variola pustulosa hæmorrhagica and purpura variola, depending upon whether the hemorrhagic manifestations appear after or before the pocks. The peculiar features of these forms are discussed.

Two forms of rashes were seen in the cases of smallpox, the initial and the secondary rashes. Two forms of initial rashes were observed: an erythema, which usually appeared on the second day of the disease, and which varied from a mere flushing of the face to a general erythema, occurred in 16 cases; the petechial form, which seldom occurred unassociated with erythema, was seen in 10 cases.

Of the secondary rashes, also, two forms were seen; a fine, red, maculopapular eruption and a mottled erythema. The first mentioned usually appeared soon after the climax of light cases of variola, while the second form occurred in the course of the more severe types, usually about the thirteenth day, and was preceded by constitutional symptoms. This mottled erythema was at first regarded as a secondary scarlet fever, but further evidence was against this assumption.

The Changes Produced in the Hæmolymph Glands of the Sheep and Goat by Splenectomy.—WARTHIN, in the contributions to *Medical Research*, dedicated to Victor C. Vaughan, June, 1903, reports a series of experiments upon sheep and goats in which the changes produced in the hæmolymph glands by splenectomy were studied. Eight animals were used, and autopsies were performed from twenty-four hours to five months after the removal of the spleen. The author finds that after total splenectomy in the sheep there is no evidence of regeneration of the primitive spleen or of the new-formation of splenic tissue. According to his observations the structural changes following splenectomy are: hyperplasia of existing lymphoid tissues, transformation

of hæmolymph nodes into ordinary lymphatic glands, and a new-formation of hæmolymph nodes out of the lobules of the fat tissue, and a later proliferation of the red marrow. He finds no evidence of the formation of red blood cells in the lymph nodes after splenectomy. The function of hæmolysis, however, is taken up first by the hæmolymph node, and later by the ordinary lymphatic gland.

The author considers that the hæmolytic function of the hæmolymph glands and hyperplastic lymph glands exceeds that of the primitive spleen, causing an excessive destruction of red cells. The resulting anæmia is later compensated for by an increased activity on the part of the bone-marrow. It would appear, therefore, that the removal of the spleen leads to an increased production or retention of some hæmolytic agent usually disposed of by the spleen. The effect of this hæmolytic agent is either to stimulate the phagocytes in the hæmolymph glands to increased activity or to change the red cells so that they are more easily destroyed by these phagocytes.

The greater number of eosinophiles found in the glands showing great destruction of red cells, the author considers to point to some relationship between these cells and hæmolysis.

The work confirms the observations of several former experimenters, all of whom, however, put different interpretations upon the appearances which they found to follow splenectomy.

Thirteen photomicrographs show the principal changes described.

A Comparison of the Animal Reactions of the Trypanosomes of Uganda and Congo Free State Sleeping Sickness with Those of Trypanosoma Gambiense (Dutton).—THOMAS and LINTON (*Lancet*, 1904, i., 1337) have found from inoculations of these three types of organisms in mice, guinea-pigs, rabbits, cats, puppies, goats, donkeys, and monkeys that the trypanosomes found in (*a*) cerebrospinal fluid of Uganda sleeping sickness, (*b*) cerebrospinal fluid of Congo Free State sleeping sickness, (*c*) blood of Uganda trypanosome fever cases, and (*d*) blood of Congo Free State fever cases, are all identical in animal reactions and morphology with trypanosome gambiense (Dutton). They believe the specific name gambiense must for the future include the trypanosomes from the above-mentioned sources. Further, there seemed to be no immunity against infection, and no transmission of immunity to offspring. Animals which seemed to have recovered showed months later parasites once more.

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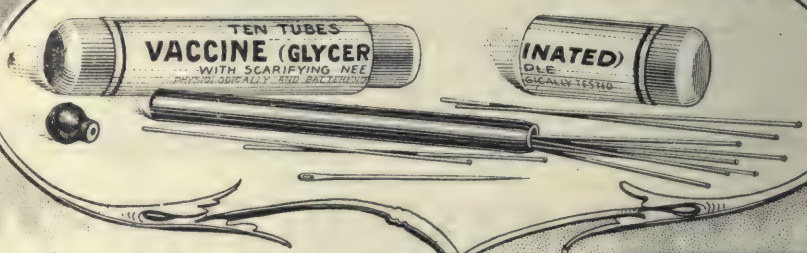

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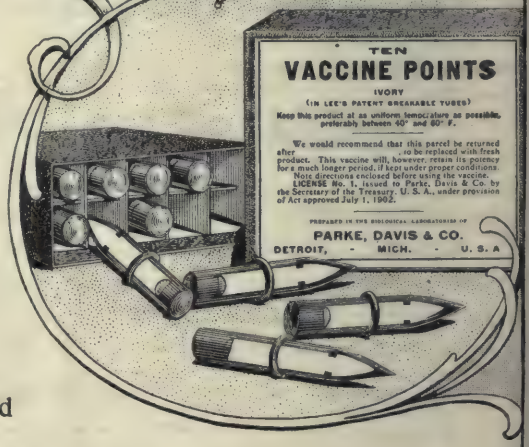

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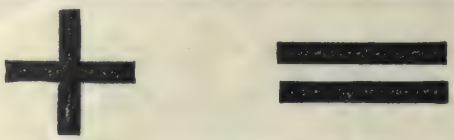

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